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A graphic representation of electrophysiologic research into vertebrate muscle movement.

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COMMENTARIES

A New Name, a Broader Mission, a Wider Audience

A scientific journal representing the Rhode Island Medical Society has been published at monthly intervals, without interruption, since January 1917. Prior to that date the Society supervised the editing of the Providence Medical Journal, a bimonthly publication which had begun in 1899. Under a variety of names and formats, then, the Society has provided its membership with a scientific platform from which medically oriented observations, interventions—even speculations—might be shared with the larger health care community. As the ramifications of governmental health policy intersected increasingly with the private practice of medicine, the journal also reflected the Society's political stands.

In recent decades, medicine has become hugely successful in its primary mission: to enhance the quality of life and to prolong survival. But medicine has also become substantially more complex. In Rhode Island, now, we have a young but scientifically vigorous medical school which has assumed the leadership at all levels of medical education as well as the sole administration of statewide residency training programs. And there is now an outstanding Department of Health which plays an increasingly critical role in the diagnostic screening of human disease, in the establishment of realizable health goals, in the maintenance of an archive for statewide epidemiologic data, and in the fulfillment of all of its conventional sanitarian responsibilities.

For years now, our editorial board has debated whether the structure and purpose of the journal was keeping up with the rapidly evolving changes in health; and it has concluded that certain changes were now necessary.

While this publication remains the property of the Society, the Board recognized the wisdom of enlarging itself by increasing the representation from the Department of Health and Brown's medical school. These new members will be selected, respectively, by the Director of the Department of Health and the Dean of Medicine. And to reflect this broadened base, we have elected to change our name to ***Medicine and Health / Rhode Island.***

Those readers who inspect the numbers in the journal's annual demographic profile of the practicing physicians of Rhode Island, will have noticed that Brown's medical school now surpasses both Tufts and Harvard as the leading source of this state's complement of physicians. Since many current Brown medical students, years hence, will be establishing their practices within the state, the Editorial Board has decided to distribute on a monthly basis, copies of the journal to all Brown medical students.

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* * *

Evolutionary Morphology at Brown: What's it all About?

G. E. Goslow, Jr., PhD

One afternoon about 18 months ago, Dr. Stanley Aronson and I were visiting and the conversation turned to the anatomy class that had just vacated Eddy Auditorium to begin a day of dissection in the morphology laboratory. Stan asked me a couple of questions about our approach to teaching and I guess I started getting a bit animated as I reviewed the morning's events. After waiting politely for me to finish, he reached over, gently touched my arm (forearm, antebrachium) and said, "Ted, I think the medical community of Rhode Island would be quite interested in knowing what is going on in anatomy at Brown these days. Would you consider putting together a special issue of Rhode Island Medicine devoted to what the morphology group is up to?" In a moment of weakness, no doubt precipitated by my enthusiasm for what our group was doing that day (or from inhaling volatile fumes for many years), I agreed. It has been fun. To celebrate our fifth year as a new group at Brown, we offer you this issue; we hope you will find it enjoyable and informative.

In 1989, concomitant with a general reorganization of the Division of Biology and Medicine at Brown University, a decision was made to assemble a group of evolutionary morphologists. To accomplish this, Brown created three additional tenured or tenure track positions in what is now the Department of Ecology and Evolutionary Biology. Within this department of ten evolutionary biology faculty, four constitute the evolutionary morphology group.

Our teaching responsibilities are undergraduate courses in comparative vertebrate anatomy, selected courses in biomechanics and functional morphology, and first and fourth year medical school courses in human morphology; i.e., gross anatomy. An additional mission is outreach to the hospitals and community. Hospital outreach is accomplished by assisting in various residency training programs of Brown's Affiliate

Hospitals. We have done this by teaching (Neurosurgery, Orthopaedics) or by providing facilities and materials for education in anatomy (Emergency Medicine, Plastic Surgery, Obstetrics and Gynecology, Radiology, and Dermatology). Our community outreach consists of hosting field trips in our research space for local elementary and secondary schools, colleges and technical schools in Rhode Island and Massachusetts.

From within this general framework, we chose to focus this issue on:

1) our approach to the teaching of Human Morphology to first year medical students
2) community outreach, and
3) research activities of our graduate students and faculty.

ANATOMY AND MEDICAL EDUCATION, AN OVERVIEW:

For centuries, the primary senses of sight and smell were our only window into the causes of illness and physical breakdown of the body. As only a relatively few medicinal applications were known, it made sense that our knowledge base from which to prepare for a lifetime of healing was what we could learn/teach through dissection. Until the middle of the last century, medical school was more or less synonymous with gross anatomy. In Italy, for example, the systematic teaching of anatomy by dissection had been prevalent since the early fourteenth century, with instructors using such standard guides as that written in 1316 by the physician Mondino de' Luzzi, professor of anatomy at the University of Bologna. For the next 500 years, students of medicine continued to view and study anatomy as the scholarly cornerstone of medicine.With time, our knowledge of the physiological processes associated with anatomy increased. By the late1600's, Harvey had discovered circulation and an era leading to our understanding of microbiology and sources of infection, through the discoveries of Pasteur, Lister and Semmelweiss, had begun. The time when anatomy formed the primary database of medical education had passed; room in the curriculum for other disciplines had to be made.

Until the early 1900's, physicians taught future physicians. Any basic science taught, was presented somewhat *ad hoc* as clinical training progressed. A pivotal publication by Abraham Flexner in 1910, however, set the wheels in motion for major changes that have greatly affected anyone trained in medicine or involved in medical education since.[1] Flexner's model provided for two years of basic science taught by basic scientists; followed by two years of clinical science taught by physicians. (Curiously, we are again in a medical training revolution that is tugging for change in the structure and curricula of medical schools across the country; I will outline this new thrust later.)

At least an entire year was devoted to the teaching of anatomy during the first half of this century; embryology and histology were often included. Since 1965, however, most medical schools have reduced anatomy to one semester or about 185 hours of classroom time. Unfortunately, as the time allotted for anatomy dropped from three or more years to one semester, the amount of anatomy attempted, in many instances, remained the same. As a result, anatomy has a bad rap the world over. Anatomy is considered by many medical students to be deadly dull, completely overwhelming and mind-numbing. I believe this attitude stems from two sources:

1) In their excitement to share all of the anatomy they know and love, some anatomists have simply forgotten how long it really takes to master the several levels of detail. They ask their students to learn in one semester what it has taken themselves years to digest, and

2) An unfortunate byproduct of the funding of scientists in this country since about 1950 has resulted in the staffing of anatomy departments by outstanding cell biologists, with little training in gross anatomy. These scientists are asked to teach a subject they have little interest in or knowledge about.

EVOLUTIONARY ANATOMY: JUST MONKEY BUSINESS?

As evolutionary biologists, it is only natural that we frame our view of the human body in a comparative context. Admittedly, humans are intellectually unique and possess abilities of creativity that far outstrip anything we witness among other members of the animal kingdom. But, physically, man can comfortably be classified as a mammal among vertebrates, a primate among mammals, and a Hominid among primates. In other words, man's physical and physiological state is the product of millions of years of natural selection exerting its influence on the genetic variation of man's ancestors. The result of this is what we perceive our physical being to be today. An appreciation of this has the effect on students of replacing a frosted window, through which a seemingly limitless number of anatomical structures remain obscure, by a crystal clear pane that allows focus on an understandable few. It hasn't always been this way.

Long before we possessed a context in which to understand the diversity of life that surrounds us, we were intellectually engaged in trying to put the many kinds of plants and animals into some ordered arrangement (hierarchy). The comparative method was a powerful tool. Understanding nature through comparison and analogy was a strategy Leonardo da Vinci used during his inquiries into human anatomy (1487–1505). He accepted the traditional view that the interior anatomy of every terrestrial creature was essentially the same, but he also recognized differences. "To compare the structure of the bones of the horse with that of a man," he wrote, "you should show the man on tiptoe in representing the legs.[2]" Though we could see such physical similarities among plants and animals on the one hand, and their uniqueness on the other, we possessed no understanding of how such patterns could be related. Enter Charles Darwin. Darwin articulated (and documented) a few basic points, which to those who accepted and understood them, immediately gave logical insight into these observations and provided a framework within which they could be studied. Darwin recognized that within any population of organisms, there exists variation in form. This is easy for us to see among humans (moving through the streets of Providence or Boston it is not difficult to see individuality), but Darwin pointed out that the same degree of variation exists among the trees of a forest and barnacles at the seashore. This variation had not been appreciated. Second, Darwin recognized that the source for this variation was heritable, but he had no concept of the gene or the laws of Mendel (these would come later). Darwin reasoned that within the setting of their particular environment during their reproductive years, some of these variants would produce more reproductively-successful offspring than would others. Finally, Darwin spent a lifetime trying to critically identify those aspects of an organism's environment that might influence the success or failure of these variants to reach reproductive status. Collectively, he called these influencing factors natural selection.

So there you have it. Variation exists for any biological trait that has a genetic component influencing its formation. A "trait" may be morphological or a biochemical process at the protein synthesis level, physiological process at the systemic level, or behavior at the individual/population level. The precise mechanisms by which natural selection acts on variation to produce evolving populations/individuals in the patterns we observe in the fossil record and those we see around us today are fiercely debated, continuously refined, and make up the "stuff" of evolutionary biology. Nevertheless, Darwin's insights provided us with an intellectual framework for understanding how some individuals gain more genetic representation in future generations than others. It is this framework within which we cast our teaching of gross anatomy at Brown.

It would be difficult for any group of evolutionary morphologists to teach gross anatomy from any other perspective than a comparative one set in an evolutionary framework. Quite honestly, it just doesn't make sense to us any other way! I am aware that for most of you, however, the details of gross anatomy do not form the building blocks of your day-to-day practice. So let me diverge from our discussion of anatomy per se to give you a more global feel for the potential of an evolutionary perspective across the entire medical training curriculum. Within medical education in general, the stirrings to frame entire components of the curriculum in an evolutionary context have begun. In 1991, George Williams, PhD and Randolph Nesse, MD teamed up and wrote a review article entitled "The Dawn of Darwinian Medicine"[3]. George Williams is a highly-respected evolutionary biologist and author of an influential book that many of my generation cut their teeth on in graduate school in the 1960's entitled *Adaptation and Natural Selection.*[4] Randolph Nesse is a respected psychiatrist who has published many papers that consider various psychiatric disorders in an evolutionary context[5–8]. In their 1991 paper, Williams and Nesse pointed out that while evolution by natural selection has long been a foundation for biomedical science, it has recently gained new power to explain many aspects of disease and mental illness. They considered infection, for example, in light of host parasite contests, and discuss who may be the beneficiary (host or parasite) of the symptoms associated with infection. Mechanical injuries and associated swelling and pain are discussed as optimal for Stone Age conditions. For example, an evolutionist might ask what component of swelling and pain of a sprained ankle is incidental to the trauma, and to what extent is it an adaptation to immobilize the joint in favor of healing?

Toxins are considered from a fascinating perspective. Arguments center on the notion that we as humans like diverse diets and as a result, we can and will eat plants that possess toxins. Why do plants contain these toxins? Plants defend themselves against herbivores mainly by synthesizing toxic chemicals (the resins of trees discourage insects from making the wood a tasty meal). The complex chemicals that make coffee so appealing are toxins that protect coffee seeds from insects and small mammals. We can safely consume vegetables and even coffee because we have evolved effective detoxification mechanisms. Since we like diverse diets, we will eat small amounts of a variety of these toxic plants and our evolved detoxification mechanisms will handle them effectively. If, on the other hand, we eat excessive amounts of those toxins that were scarce during our evolutionary history (e.g., pesticides, nickel and mercury), we are in trouble. Evolutionary arguments to explain morning sickness during pregnancy and allergic response also are discussed.

Williams and Nesse consider genetic diseases in light of the selection of genes that may be favorable for the attainment of reproduction but not so subsequently. They propose that the diseases of aging may be particularly associated with genes selected for early benefits. Finally, a substantial part of the paper is devoted to a consideration of the idea that human biology is designed for a Stone Age environment. In 1986, Endler[9] articulated what is implicit in evolutionary theory: Adaptations are produced and maintained only in the range of environments in which selection takes place. For early humans, the socioeconomic environment consisted of small groups hunting, gather-

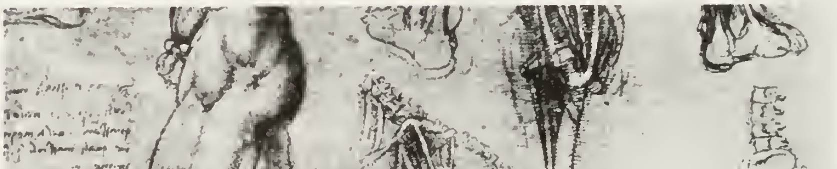

Figure 1. Leonardo da Vinci's passion for comparative anatomy and human anatomy is ubiquitous throughout his sketches and notes. On folio 22 recto of the fifth Quaderno, the pelvic limb of a rearing horse is compared to the lower limb of man, with the note: "Of the relationship that exists between the arrangement of the bones and muscles of the animals and that of the bones and muscles of man. To compare the bone structure of the horse with that of a man you should show the man on tiptoe in representing the legs."

ing, mating, raising children, and responding to threats and opportunities provided by neighboring groups. The unique ability to use culture to adapt to diverse and changing environments enabled human populations to grow enormously, spread widely, and adapt technologically to a great range of conditions.[10]

Sounds interesting, doesn't it? If my excerpts have touched upon your particular specialty or interests, you can appreciate the power of an "evolutionary perspective" as an organizer of detail. There is no question that medical school curricula across the country will respond in one way or another to the 1991 article of Williams and Nesse. Articles and books have been forthcoming and will no doubt continue to appear at an accelerated rate for sometime. Two published in 1994 are particularly relevant here; Nesse and Williams *Why We Get Sick*[11] and Paul Ewald's *Evolution of Infectious Disease.*[12]

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Anatomy and More

Lucile F. Newman, PhD

Anatomy has traditionally been viewed as shock treatment for the young man or woman entering the precincts of medicine, a threshold that medical school is to be different from anything one had experienced before. Legend dictates that one becomes transformed in the learning of anatomy, becoming a different person when learning those morphological elements of life and death revealed only to those about to be initiated.

Early in the history of Brown's medical school, over two decades ago, two medical students "having been through Anatomy," sought medical faculty help in designing a companion course to human morphology, a course which they believed would broaden and extend the study of anatomic dissection by creating exercises forcing the student to perceive the human body in ways other than how it is usually portrayed in dissection manuals. This elective educational experience, designed by these two students, was unlike any medical school course that anyone could recall. The fundamental principle governing this exercise was as follows: As medical students undertake the study of the normal morphology of the human body they would be helped if they were to consider, in parallel, the human body from other, perhaps more esthetic, humanizing, cross cultural and active learning perspectives.

The course was regarded as complementary rather than as an alternative to the required course in anatomy and was therefore designed to explore varied possibilities in perceiving the human body. The course met for at least three hours a week; the participants included about one third of the first year medical school class, the Professor of Anatomy, the Dean of Medicine as well as other deans and faculty (both medical and nonmedical).

The first few sessions were conducted by Brown's Art Department and involved life drawing from live models. It was a challenge to those participating since it demanded a recruitment of talents and skills not customarily encouraged in conventional medical education. To many of the students it was a disquieting experience. "We had to create a body rather than take it apart," said one student.

Subsequent classes included esthetic exercises conducted by rehabilitation specialists, using live music; a series of ballet classes exploring interactive dance patterns; student participation in a theatrical performance centered on aging; and sessions devoted to music and songs from many countries dealing with body perspectives, set in a cultural context. "We have bodies, too," said one student in wonderment.

This educational experiment sought to challenge the students' sense of wonder and capacity to retain structural information, as well. It sought to extend the study of human anatomy by illustrating that bodies move as well as remain stationary; that the body possesses great esthetic beauty and awesome individuality — even those taken apart by the learning medical student.

The experiment lasted but one semester since neither funding nor continuing leadership were available during the growing years of this medical school. Those who participated, however, remember it to this day as a joyous affirmation of the human body.

Dr. Newman is professor of community health and anthropology at Brown University.

Navel Encounters

Stanley M. Aronson, MD

To the anatomist, the umbilicus (omphalos) is but a puckered scar involving ventral abdominal skin and underlying linea alba, a remnant of the fetal umbilical orifice following its physiologic closure at birth. It performs no function beyond birth except as an occasional object of sexual interest; it is gender-neutral, and, other than an occasional hernia (omphalocele), causes no appreciable disability or disease. Yet this banal midline cicatrix manages to capture the imagination of both children and adults: to children, it is a source of innocent wonder and amusement; and to adults, it persists as a symbol of centrality that permeates their most basic cosmologies.

This inconsequential abdominal scar, sometimes convex and sometimes concave, is present in all creatures which require a placenta for prenatal nutrition. Thus, it exists in all mammals (except, of course, for Renaissance art renditions depicting the unclothed Adam and Eve.) The words which define this scar, as with so many anatomic terms, fall into two categories: the vernacular (eg, belly button, navel, pupik) which are of Germanic or Slavic origin; and the professional (eg, omphalos, umbilicus) which are of Greco-Roman origin.

The *omphalos* was the name given to a hemispheric stone in the shrine of Delphi at the site where Apollo had slain the evil serpent Python. To the ancient Greeks, this sacred mounded stone represented the site of a primordial battle, a revered tomb as well as the hallowed center of all creation; and were this stone to be removed, they feared the world would surely descend into chaos. The Pole Star, around which the firmament revolves, is the celestial counterpart of omphalos. Indeed, there are many northern cultures, such as the Lapps, which call this star the navel of the heavens.

The mother of Tantalus and queen of the Lydians bore the name Omphale. It was she who purchased Hercules as a slave. (Hercules had unjustly murdered Iphitus. In despair he appealed to the oracle who told him that expiation would be forthcoming only if he were sold into slavery for one year.) Scholars have pointed out that the Greeks identified the navel as the seat of female passion and that Hercules' enslavement (during which time, incidentally, he fathered three of Omphale's children) represented nothing more than the exercise of Omphale's carnal passion. But other scholars have claimed that the debt of Hercules was really to the Delphic oracle and that the confusion over names led subsequent archivists mistakenly to assign his servitude to Omphale the queen rather than omphalos the sacred stone.

The Rig Veda, oldest and most hallowed of the Hindu scriptural texts, describes the center of all things as Vishnu's navel from whence arose both the eternal lotus (where Brahma was born) and the seeds of all living things.

Buddha sat upon such a motionless hub of the world when he achieved ultimate enlightenment at Bodhgaya. In many African cultures, the ruler also sits upon a small mounded stone, the focal point from which arises his power and authority. Even the kings of England possess a sacred stone (the Stone of Scone) which rests beneath their coronation throne. All of these mythic components share a common feature: a primeval stone, metaphorically a navel, which is cherished because it is believed to identify the hub, the center, the font of all things and from which emanates all power and all of life's vitality.

In Genesis, Jacob goes forth to seek a wife. Along the road to Haran he rests for the night taking a stone for a pillow. During the night, he dreams of a heavenly ladder complete with angels, and from the top of which the Lord speaks to him. When Jacob awakens, he exclaims: "How awesome is this place ! . this is the gateway to heaven." He then consecrates the mounded stone with oil, naming it Bethel (House of God). (Genesis 28:11-19.) Historians have equated the many biblical Bethels with the omphalic stones of other cultures, each purporting to represent the hub from which all celestial activity arises. In classical Hebrew the word *tabbur* signifies both the navel and the midpoint of the world.

But what once had been revered as shrines gradually transformed themselves into symbols of idolatry. Just prior to their arrival in Canaan, the Lord commands Moses to instruct the Israelites to destroy all figured stones (Leviticus 26:1; Numbers 33:52.) And in the prophetic testaments, such stones are now equated with graven images and to be condemned. The pre Christian Irish had also venerated a special stone (at Cromm Cruaich) as the center of their world; yet with his staff St. Patrick destroyed it, reinforcing the contention that all forms of geomancy are repugnant to Judeo-Christian belief.

There is something eminently eternal and reliably solid about a stone; and at unsettled times and junctures, it is therefore not surprising that some have been endowed with majestic power. Some, too, have also been considered as the center around which all life revolves a kind of geo-egocentricity. What is puzzling, though, is how these sacred omphalic stones became so indelibly associated with the human navel. There is nothing particularly stony, awesome or even enduring about the navel. It is, however, visible to all as the center of the body, midway between the flanks; and midway, too, between the scalp and toes. It is as though the Creator had designed a specific structure whose sole purpose is to say, "By this mark know that I am your center, the beginning and continuing core of your being; and through this portal I once sustained you through your primordial months of utter dependency." And somewhere in the dim recesses of early Greek history the word for navel was then transferred to a revered stone; or, perhaps, it was the other way around and the stone's name was bestowed upon the navel.

Staring at one's knee or wrist, for the sake of staring, sounds bizarre; but gazing at one's navel is commonplace, so common that the Greeks devised a special word for it (omphaloscopy) and in many societies, uninterrupted navel-gazing is considered the quickest pathway to inner peace. Indeed, there is a sect of anchorites, the omphalopsychites, who regularly stare at their navels to reach tranquility.

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1990—1995, Human Morphology at Brown: It's All in the Team

G.E. Goslow, Jr., PhD

It is the best of times. The 1990's are an exciting time to be teaching gross anatomy in this country. Young people are interested in their own physical fitness now more than ever before and with this comes interest in nutrition and exercise. In addition, humans have always been interested in their origins and new discoveries in anthropology are being announced each week. Finally, the sheer beauty and clarity of anatomical structure made available to us through the high-tech imaging techniques such as computer aided tomography (CT) and magnetic resonance imaging (MRI) have had a positive effect. Not only are clinicians from a diversity of subspecialties suddenly eager to try their skills at picking up a ligamentous tear or the first signs of a tumor from one of these images, but any student with interest in the living world is stopped cold by the esthetic quality of an MRI's depiction of biological structure. In teaching anatomy at Brown, we continually try to capitalize on these natural areas of interest and curiosities of our students.

It seems appropriate at the outset to share some of our teaching philosophy with you. Since I am writing this section, I suppose my own viewpoints are likely to emerge most clearly, but I will also attempt to encapsulate the philosophy of my fellow teachers. Throughout my teaching career I have felt privileged to have known many talented young people. The Brown medical students are no exception; they bring special gifts to us along with a refreshing attitude and high hopes for a bright and exciting future. I know that as teachers we must be careful to nurture this enthusiasm and provide an environment where it will grow. I am convinced that effective education goes far beyond the material content dispensed in the courses we teach. I am a firm believer that perhaps the most lasting and important effect we have on students comes through their perceptions of what we think about them and our attitude toward the subject. If students perceive that we have time for them, that their ideas are important and that we are excited about sharing our subject with them, they too will catch the spirit and rewards of learning.

Our gross anatomy course at Brown is a team-taught course. Any educator will tell you that from both a teaching and student standpoint, a team-taught course can be deadly. You know the symptoms: a dominance of one personality one week followed by long periods of absence, loss of important detail (as in forgetting to assign the spleen), teachers who can't remember students' names and students who can't remember teachers' names, and perhaps the most prevalent — a parade of favorite research topics with little continuity. We work hard to avoid these pitfalls and with the assistance of some perceptive co-educators, I think we have succeeded. The three of us whose primary responsibility is to teach anatomy are privileged to have shared the teaching forum with some outstanding co-workers. Our co-workers form the heart of what we do and since 1990, these people have been exceptional. So exceptional in fact, that any success Human Morphology has enjoyed is truly a tribute to them. Our immediate colleagues who work with us daily to keep the course moving are a Postdoctoral Teaching Fellow and graduate students from our Department of Ecology and Evolutionary Biology. The two Postdoctoral Fellows for the past five years, Dr. Alan Sokoloff and Dr. Ernie Wu, have been truly dedicated to the educational process, deeply committed to students and each has served as an important role model for the rest of us. Our graduate student co-teachers have done exemplary jobs as well. Each has brought special talents and each has contributed to our overall effort in a positive way. We are pleased to have had the opportunity to work with Dr. Tricia Wilhelm, Dr. Ron Meyers and Ms. Tracy Popowics who helped get the program underway. And most recently, we have had the pleasure of working with and learning from our three present co-workers, Ms. Kay Earls, Ms. Jennifer Gray Chickering, and Mr. Dale Ritter.

> *The trick is to encourage students to gain a command of as much anatomy as they can comfortably handle without short-circuiting their brains and turning off their interest in anatomy forever.*

THAT "KILLER COURSE," GROSS ANATOMY

At Brown, gross anatomy is entitled Human Morphology, an appropriate title we inherited in 1990. "Morphology" captures the notion that we stress more than just structure but also include function wherever we can. A useful experience in gross anatomy requires long hours in the dissection laboratory. We recognize this and have structured our course to maximize the quality of the time spent in the laboratory. Scheduled classroom time for formal lecture is only two to three hours/week, whereas about 16 hours/week are devoted to the laboratory. Students have free access to the laboratory outside of class time and are able to establish their own schedules to some extent.

Eight hours of laboratory at a stretch is a long time. We have discussed spreading the course over three afternoons each week, but students seem to prefer the two days of "total immersion." "Even though we are pretty beat by three in the afternoon, that's okay because we don't even have to try to get anything else done on Tuesdays and Thursdays. Anatomy is all we can do and that somehow makes our lives less complicated."

ABBREVIATIONS USED

ACL	Anterior cruciate ligament
ADAM	Animated Dissection of Anatomy for Medicine
ATPase	Adenosine triphosphatase
CT	Computed tomography
ERCP	Endoscopic retrograde cholangiopancreatography
GI	Gastrointestinal
MRI	Magnetic resonance imaging
RIH	Rhode Island Hospital
RISD	Rhode Island School of Design

To help alleviate the tedium of the long day and take advantage of the opportunity to work with students in small groups, one instructor (and perhaps a second) prepares a prosection and works with four-eight students throughout the day. These prosection sessions serve several functions: to orient the students in anticipation of their starting on a new area, to illustrate the specifics of an anatomical system, or to extend or clarify what has been learned through their own dissections. The prosections (about 20–30 minutes) also provide students with the opportunity to ask questions and discuss whatever comes to mind.

A glance at *Gray's Anatomy* reminds us that every structure in the human body that can be seen has been given a name, or so it seems. Of course a student who can learn all these names, recognize a structure on sight and know its three-dimensional relationship to other structures around it, will undoubtedly be an accurate, and perhaps, effective physician. On the other hand, we recognize the near impossibility of accomplishing this in a one semester course in anatomy. The trick is to encourage students to gain a command of as much anatomy as they can comfortably handle without short-circuiting their brains and turning off their interest in anatomy forever. Critical to achieving this goal is to help the students get beyond just confronting the material but to engage and work with it as well. We attempt to do this during our lecture and laboratory sessions wherever possible, and students also accomplish this through their prosection/demonstration.

ENGAGEMENT NOT CONFRONTATION

Our lectures generally do not emphasize specific anatomical structures, rather we attempt to provide a developmental, functional or evolutionary context for the material being explored — an approach that has proven very effective. Students are captivated by Professor Sharon Swartz as she unfolds the organization of the head and neck from a developmental perspective set in an evolutionary framework. Her discussion of the formation of the aortic arches and the innervation fields of the trigeminal, facial and glossopharyngeal nerves as these relate to the branchial arches not only provides a solid and logical framework for the anatomy, but makes a comprehensible story which medical students can take with them into the clinics and remember forever. To observe Professor Dave Carrier develop an evolutionary timeline on the blackboard and then proceed to help students gain a new appreciation of the organization of man's cardiovascular and musculoskeletal systems for the design of a bipedal runner is exciting to behold. Dave reminds the students of this timeline throughout the course to help them understand the organization and limitations of our digestive system and why certain diets are beneficial while others are harmful.

STUDENT PROSECTION/ DEMONSTRATIONS

"That was amazing." "What an impressive dissection; it was the cleanest exposure of the circulatory tree in the neck I have ever seen." "What a great explanation of the evolution of bipedality that was." These are some of the comments made time and time again by the immediate teaching staff and a visiting critic or two following a student's presentation at the dissection table. The students' prosection/demonstrations, which focus on a region of anatomy the students have been dissecting, are centered on some clinical, functional or evolutionary point. The presentations must be supported by select primary sources from the basic science and/or clinical literature. We use this aspect of the assignment as an opportunity to help those students who need it to discover the primary literature and learn how to evaluate it. The prosection/demonstrations not only provide an effective way for students to engage and learn the material, but it helps them prepare for the clinics, where they must effectively communicate with their peers and patients on a daily basis.

Prosections are prepared to illustrate and/or clarify particular anatomical features. Prosections also provide us an opportunity to work with students in small groups. Here Jennifer Marler, MD (right) a plastic surgery resident, explores a point with Kathy Lin (left) and Chad Lamendola (center).

"It's 5:30 p.m. and you have been here since noon. Are you ready to go home yet?" "No" is usually the response from the visiting critic. Although the student prosection/demonstrations are relatively short (10 minutes with 5 minutes for discussion), the students jump at the opportunity to present and put substantial effort into their presentations. To reward this effort and add a 'bit' of "class" (and excitement), we invite visiting critics to stand with us. Most of our visiting critics are physicians from the Brown community; each has amazing stamina. The sessions usually go on for hours. The presentations are enthusiastic, thoughtful and informative. We invariably come away ex-

Abeel Mangi (left) and Rudrani Banik (left) discuss their prosection with instructors Dale Ritter (right, back), Jennifer Gray Chickering (right, middle), and Ernie Wu (right, front). Jim Greenspan, MD (center, foreground), a neurosurgery resident and visiting critic, listens intently on what is being presented.

Jim Greenspan, M.D. (left) and instructor Jennifer Gray Chickering (center) enjoy a lighter moment during Rudrani Banik's prosection/demonstartion.

hilarated and refreshed. Each student is evaluated for anatomy demonstrated, dissection technique, outside resources, organization, presentation, and effort. A consensus evaluation is arrived at through discussion following each presentation and written comments are prepared and given to each student shortly after his or her presentation.

We gratefully acknowledge the tireless hours the following visiting critics have given us since 1990: Jim Greenspan, MD, Dean Gobo, MD, Neville Knuckey, MD, Mark Mittler, MD, Larry Proano, MD, and Mark Ridlen, MD, all of Rhode Island Hospital; Farish Jenkins, Jr, PhD, Harvard University; and Cathy Shannon, MD, Memorial Hospital of Rhode Island.

VISITING SPECIALISTS

We made a decision early on to provide some clinical relevance to the material the students were learning. In addition, we wanted to expose students to the numerous options that are open to them as practicing physicians. Of course they have some understanding of what a life devoted entirely to patient care is all about, but many have never considered research or teaching. Among our visiting specialists, we bring in clinicians with strong research programs as well as clinicians with major responsibilities divided equally among teaching, research, and patient care. Basic scientists with research programs that directly affect human health also participate. The teaching forum of our visitors varies from a one hour lecture followed by a second hour of questions and discussion to five to six hour sessions in the laboratory, working with the students in small groups. Following these presentations, there is time for students to interact with our guests informally over refreshments. When possible, four to five students are given the opportunity to engage the guest over a leisurely lunch.

Use of a student's shoe and striking illustrations on the board enable F. A. Jenkins, Jr to intellectually engage the students as they consider normal and pathological gaits.

Lecture/discussion—We meet at 9:00 am. The last of the students arrive at 8:59 am, scurrying to reach a seat so they do not keep the speaker waiting. The special guest is introduced and their professional pedigree/accomplishments given in a traditional way. We attempt to share with the students some insight into the path taken by the guests in achieving their own professional goals. This is done particularly for those students struggling with their own identities and future course.

During the next 90 minutes or so, our visiting specialist may take time to review a particular surgical procedure which relates to, or incorporates, an area of anatomy recently learned by the students. (See M. Felder's article). Another may review a few relevant anatomical features as a prelude to a lively question and answer period regarding ethical questions such as artificial insemination, surrogate mothers and single parent pregnancies. Students and teaching staff alike, sit fascinated and totally engaged during such discussions. We have been treated to exquisite demonstrations of the structural and functional fundamentals of human gait and we have had pathologies of gait demonstrated to us with such pedagogical elegance that time will never erase them from our memories.

In these lecture/discussion formats, we have been forced to stretch to the limit our knowledge of the gross anatomy of the brain as we were told by a basic scientist of the behavioral compensations of the patients he studies who have undergone corpus-callosotomy to control severe epilepsy ('split-brain patients'). We have witnessed the thought processes of a clinician active in both the basic science and clinical trial aspects of treatment for torn menisci or a ruptured anterior cruciate ligament (ACL). We have learned of the potential advantages of non-biological prosthetics for ACL replacement from a representative of a leading biotech company. Evidence for the cause of thoracic outlet syndrome, which is not induced by a cervical rib was passionately laid before us; indeed, our own student cadavers were measured to gather evidence for this phenomenon.

When the day is over and our guest gone, some of us engage in vigorous debate over the issues raised and some, I am pleased to add, head for the library to dig out related literature.

Participants come to us from institutions as far away as Vancouver, British Columbia, and the Mayo Clinic. We have had numerous visiting specialists participate in the lecture/discussion format (some more than once) since 1990. We are most pleased to acknowledge the support and participation of the following: Allan Deutsch, MD, Martin Felder,

Following a thought-provoking *lecture/discussion* by Laura Nevel, MD (right), Dan Theodoro (center) and Julie Farley (left) take the opportunity to ask specific questions and follow-up their own ideas.

John Cronan, MD (left) joins the class early in the semester to begin assisting students in the process of transferring knowledge gained through dissection to a two-dimensional image.

MD, Laura Nevel, MD, and Stan Simon, MD, Miriam Hospital; Paul Fadale, MD, and Jennifer Marler, MD, Rhode Island Hospital; F.A. Jenkins, Jr., PhD, Harvard Medical School; Michael Joyner, MD, Mayo Clinic; G. R. Mangun, PhD, Dartmouth Medical School and the University of California, Davis; William Nelems, MD, and Darlene Redenbach, PhD, Vancouver Hospital; R.A. Settlage, MS, Gore Associates, Inc.; Eric Webber, MD, Nova Scotia.

Clinical prosection/demonstration Five to six hours. This section begins at 11:00 am. Material is reviewed four to five times and we finish around 5:30 pm — exhausted, but elated too. The clinical prosection/demonstration has proven to be an extremely effective way to reinforce from a clinical perspective the anatomy students have learned. The visiting clinicians make it work and are unselfish in the time they spend. Students are brought from the main laboratory in small groups, provided with refreshments and a few moments of relaxation, and then engaged in one way or another by our guest. Again, where appropriate, the guest is asked to provide a thumbnail sketch of how they ended up doing what they do. The teaching staff are quick to arrange for their own opportunity to listen in.

Early in the semester, through the careful guidance of participating radiologists, students begin to transfer what they have learned in dissection to the incredible world of imaging (See JL Cronan's article). One skilled clinician with expertise in the use of Doppler flow techniques for diagnosis of blood flow abnormalities easily captivated all of us by using a combination of illustrations, tapes and dynamic images from clinical cases. Through the use of skeletal and/or cadaver material, guest orthopaedists have demonstrated several intuitive ways to sort out spinal nerve or brachial plexus injuries from peripheral nerve injuries. An ophthalmologist reviewed those features of the eye critical for cataract surgery and glaucoma and shared with us the thrill of restoring sight to those in underdeveloped countries. Finally, neurosurgeons have reviewed the different types of brain tumor seen through arteriograms and demonstrated the structures "which must be avoided" during endarterectomy and aneurysm repair of the middle cerebral artery. If you can recall the feelings of despair as a first year medical student when confronted with all that detail in the head and neck, you can appreciate how important a simplified but relevant clinical review can be

The "hot seat" is occupied by Calvin Lee (right). Mark Ridlen, MD (left) skillfully leads Calvin to a plausible interpretation and diagnosis of the patient whose images are before them. Christina Mitchell (front) and Danielle Viets (back) look on.

We have had numerous clinicians participate in the clinical/ prosection demonstration format (several more than once). We gratefully acknowledge the participation of the following: Deborah Benzil, MD, New York Medical College; John Cronan, MD, Jennifer Marler, MD, Mark Ridlen, MD, and Jim Williams, MD, Rhode Island Hospital; Moses Goddard, MD, Brown University; Bob Hopkins, MD, and Laura Nevel, MD, Miriam Hospital; and Cathy Shannon, MD, Memorial Hospital of Rhode Island.

Jim Williams, MD, an orthopaedics resident, clarifies some finer points of shoulder fracture diagnosis using Phyllidia Ku as his subject.

TEACHING RESIDENTS

In addition to established physicians, we make an effort to bring in residents in various stages of their training. Residents may participate in the lecture/discussion or clinical prosection/ demonstration formats or they may join us in the laboratory for several weeks. In the lab, they work with students at the dissection tables by answering questions, assisting with the location of structures, and providing a valuable clinical viewpoint. Depending upon their expertise, residents may also help the students transfer their three dimensional cadaver-based knowledge to various images. Residents provide an additional dimension to training because of their closeness in age to students helps facilitate education and profession-related discussions. We are particularly pleased to give a special nod to the teaching efforts of Dr. Eric Webber. Eric worked with us consistently for two years. His spirit and good will captured the respect of both students and teaching staff. He is presently doing a pediatric surgical fellowship at Children's Hospital, Halifax, Nova Scotia. The following resident physicians are also gratefully acknowledged for their extended assistance in the

An outstanding physician/educator, Cathy Shannon, MD, explores a variety of imaging techniques in a clinical prosection/demonstration. Arteriograms, CATscans and MRIs are viewed and discussed.

Although he may appear to be facing imminent defeat before Bill Ruth (left) and Arno Sungarian (right), rest assured that Paul Fadale, MD (center) recovered easily. Dr. Fadale's *lecture/discussion* of the anterior cruciate ligament effectively illustrated the interdependence of basic and clinical science for the effective treatment of injury.

The"in-residence" second-year medical students provide substantial instruction and positive support to the first-year students. Ray Moreno (center) makes a point to Arno Sungarian (right) and other students.

course: Karen Clark, Emory School of Medicine, Jonas Goldstein, Rhode Island Hospital; Susanna Lee, Massachusetts General Hospital; John Mungovan, Brigham and Women's Hospital.

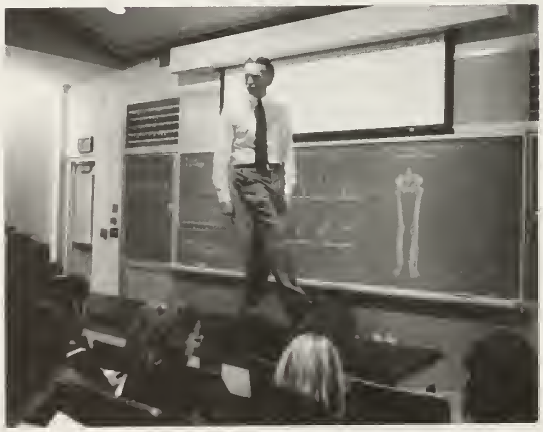
SECOND-YEAR MEDICAL STUDENTS

You can imagine our amazement and gratification when a student who has just completed Human Morphology says, "Is there any possible way I can come in next year and help teach in the laboratory?" or, "I would love to dissect next summer and help prepare some prosection material for next Fall's course. Is there a possibility?" Unbelievable, but true. You can quickly appreciate the magnitude of the message sent to a struggling first-year student in anatomy to see a second-year in the laboratory helping out or be told that the incredible dissection before them was prepared by a second-year that they may know. We are overwhelmed with this kind of enthusiasm among our students. "Of course," we say, and then try to fit everyone in. Since 1990, outstanding prosections during the summer have been prepared for us by John Saugy (resident in orthopaedics, Cornell University), Alex Meyer (fourth-year), and Abeel Mangi (third-year).

Since 1990, we have had four "in-residence" second-year medical students. These individuals form an integral part of our teaching staff during the Fall semester. Like us, they work with the students at their dissection tables, serve as resources for student presentations, hold review sessions, provide encouragement and support, and in some cases, help construct and evaluate examinations. We are grateful to Chris Breen (resident in orthopaedics at the Mayo Clinic), Paul Vargehese (resident in internal medicine, Johns Hopkins Hospital), Sara Fazio (resident in internal medicine, Beth Israel Hospital), Ray Moreno (fourth-year), Calvin Lee (third-year), and Abeel Mangi (third-year).

Many second-year students are anxious to help in any way they can, and join us as "rotating-participants." As such, they may swing into the laboratory at any time during the semester, but their primary responsibility is to assist with the dissection/demonstration of a particular region of the body (e.g., the upper arm, thorax, abdomen, head and neck, etc.). Again, the pedagogical value of having these students moving through the laboratory, assisting with specific dissections, and providing feedback to first-year students, cannot be overstated. Their participation is appreciated and valued. We are appreciative of the work of: Win Alford, John Anastasatos, Rudrani Banik, Catherine Birndorf, Eloise Caswell, Marina Catallozzi, Jack Chen, Peter ChinHong, Noel Chiu, Chris D'Arcy, Joe Diaz, Robert Grossberg, Joyce Han, Tim Hastings, Niki Hawk, Chad Lamendola, Marilyn Lawrence, James Lin, Kathy Lin, Jerome Liu, Catherine McLean, Bina Mehta, Alex Meyer, Christina Mitchell, Lisa Nadeau, Hari Naidu, Tim O'Brien, Scott Padavan, Giavana Papa, Sufala Patil, Joe Patruno, Mark Polhemus, Staci Resnick, Josh Rotenberg, Bill Ruth, Meg Rydell, John Sabra, Wendy Sears, Jonathan Siegel, Arno Sungarian, Mark Tenerowicz, Stacy Tessler, Daniel Theodoro, Michael Vaughn, Joanne Wilkinson, and Tammy Wu.

The interactive value of the clinicnal prosecution/demonstration is captured here as Debbie Benzil, MD, a resident in neurosurgery, listens to a question being asked by one of the students.



Farish Jenkins, Jr, PhD, demonstrating a point which relates to human gait. Dr. Jenkins, a professor in the Harvard/MIT Division of Health Sciences and Technology, has studied the gaits of a variety of mammals and effectively assists the students to understand man's bipedal gait within the context of its "determinants."

TECHNICAL SUPPORT

Another invaluable member of the team at Brown University is Mr. Arnis Abols. Arnis' attention to the details of the moment to moment activities relating to the laboratory component of the course, cannot be overemphasized. Arnis makes sure that all preparations used by the students are of high quality. He spends considerable time organizing the laboratory and keeping it clean and pleasant. If an anatomy laboratory gets "grimy," students will quickly make excuses to go study something else. We contend that to keep students actively engaged in learning anatomy, they must continually believe that the teaching staff cares about their situation and their environment. Arnis' role is fundamental to this perception and he constitutes an essential part of our teaching team.

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Clinical Perspectives on Anatomy

A Radiologist's View

John J. Cronan, MD

Ted Goslow contacted me in July 1990, explaining that he wanted to discuss the Brown Medical School anatomy course and gauge my interest and willingness to participate in the course. When we met, it was clear that he was motivated by a desire to make the course clinically relevant. Ted requested my involvement because he perceived that radiologists could provide the clinical background previously missing from the Anatomy Program at Brown. I was both receptive and eager to participate as were several of my colleagues from the Department of Diagnostic Imaging.

My involvement during these years has been to participate in the anatomy course by spending a day with the students. To make my session informal, the class is divided into four groups of approximately 15 students. I spend 90 minutes with each group reviewing the anatomic area most recently studied in lectures and the dissecting laboratory. Visits by radiologists are scheduled so our sessions highlight the limited anatomical region reviewed in the previous weeks. My assigned area is the chest and mediastinum. I begin by reviewing the anatomy of the chest and mediastinum using computed tomography (CT) as a demonstration tool. The fun begins as student volunteers discuss cases which I present. A clinical history is provided. Student volunteers review several x-rays and determine what is wrong with the patient. With a minimal amount of guidance, the students do a great job functioning as diagnosticians. Utilizing clinical history I create a scenario whereby the students are young physicians moonlighting in a walk-in clinic. I provide them with a brief history, an x-ray or CT, and ask them what to do next. It is startling, both for the students and for me, to realize that with common sense and a newly acquired knowledge of anatomy, a diagnosis is easily arrived at.

With Dr. John Cronan's guidance, Eowyn Rieke is able to determine what anatomical structures have been compromised by a large mediastinal tumor.

I am careful not to market radiology as a potential career. My intent is to demonstrate how primary care physicians and specialists employ a knowledge of anatomy in everyday clinical practice. At noontime, four or five students take me to lunch. During this session, the discussion focuses on the future of medicine. My expected role is to "accurately and succinctly" describe what medicine will be like in ten years. Even at this state of their training, issues regarding the future of medicine are of concern to these students.

The Rhode Island Hospital Department of Diagnostic Imaging has also offered students the opportunity to visit on weekends during the Fall semester. Two students join the staff and residents participating in the readout sessions that occur in CT, MRI, and ultrasound. Students have responded to this opportunity enthusiastically. The sessions are extremely busy. Often 40 CT's and 20 MRI's are reviewed in five to six hours. For students, these clinical sessions provide an opportunity to work with residents and fellows in radiology and to see a tremendous amount of anatomy and pathology displayed via imaging. The sessions reinforce the anatomy that they have just learned and integrate it with clinical medicine. With the passage of time, I routinely encounter third- and fourth-year students who participated in this weekend program. They have commented about how interesting this experience was and how it helped them understand the importance of their studies. Exploring CT's of the chest, trauma abdomens, CT's of pancreatic masses and MRI's of brain tumors, has made their studies seem more pertinent.

> *With a minimum amount of guidance, the students do a great job functioning as diagnosticians.*

Brown University School of Medicine is extremely lucky to have its present group of morphologists. They are conscientious anatomists with special expertise in Evolutionary Morphology. They complements their skills by inviting physicians to participate and provide a clinical focus to the anatomy course. The integration of a clinical perspective into the first-year medical student program strengthens the students' level of understanding and learning and is an exciting development in the curriculum.

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A Surgeon's View

Martin E. Felder, MD

The Brown Medical students of the 1990's seem well prepared and enthusiastic about anatomy. I have been asking third-year clinical clerks the same anatomical questions for over 20 years and recently have noted that I am getting better answers. It is not that their responses are just more spontaneous or correct, but I have seen improvement in the ability of the present students to recall what they have learned. The minimal prompting required shows that they have a firmer foundation of knowledge than ever before.

A firmer foundation of knowledge! What is the cause? I'd like to say that the students are brighter than ever but at Brown we have always been blessed with gifted young men and women. My guess is that with the coming of so much new "imaging technology", along with the presentation of some clinical perspectives in Human Morphology, the subject of anatomy has taken on renewed interest.

Why has the study of anatomy become more important? The body has not changed. But our access to it has. With the advent of newer diagnostic studies such as ultrasonography, CT scanning, MRI and arteriography, there is hardly a field of medicine in which there is not an increased interest in anatomy. We all want to know what we are looking at when the radiologist reviews our films. We want to see and understand the extent of pathologic change and the involvement of structures by the disease process. Anatomic alterations provide us with diagnostic, therapeutic, and prognostic information. The more that our students understand this, the more interest they will have in the subject.

I am just one of the physicians who assists in stimulating interest in anatomy by using the lecture discussion format relatively early in the semester. My lectures use complicated surgical problems that involve several anatomical structures. A patient with carcinoma of the pancreas is presented. The symptoms due to obstruction of the bile duct, pancreatic duct and duodenum are discussed. Alterations in digestion are mentioned, and even though the students have not yet covered the physiology of digestion, they ask many intelligent questions. Diagnostic studies are reviewed, which may involve an upper GI series, a CT scan and ERCP (endoscopic retrograde cholangiopancreatography).

During a *lecture/discussion* Dr. Martin Felder fields one of the numerous questions posed by the first-year students.

The body has not changed. But our access to it has.

A step-by-step resection of the tumor is then proposed and undertaken. The Whipple operation (radical pancreaticoduodenectomy) involves many structures. The removed tissues include the gastric antrum, the distal common bile duct, often the gall bladder, the entire duodenum, and the head of the pancreas. The arterial supply from the celiac axis is reviewed, as are the venous pathways that lead to the formation of the portal vein. One would think that the students would be overwhelmed part way through the presentation but they are not. They follow closely as I explain how we reconnect the stomach, bile duct, and pancreas to the intestinal tract.

A question and answer period follows. It lasts for over one-half hour and when we stop we have not had enough time to answer all of the questions; and the questions are good. They show that the students have been paying attention and that their minds have been stimulated by the material discussed.

The entire session is made more valuable because the anatomy of the area has been taught prior to my lecture. Thus, my role is to coordinate and to review, and, in a way, to make the material "come to life." We are optimistic that this method benefits the students. I know that the clinicians who are involved in this program thoroughly enjoy their participation.

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Additional Teaching Amenities in Morphology

Ernest Wu, PhD and
G.E. Goslow, Jr., PhD

In addition to an effective teaching team, we strive to provide an environment in the laboratories which is conducive to the long hours spent either dissecting, studying or interacting. By adding a few hanging plants, hanging posters that show the dynamics of human form in dance or athletics, splashing on a bit of fresh paint, and encouraging the students to"sign the walls" when they complete Human Morphology, we have considerably brightened a basement space void of windows. We gratefully acknowledge that the Dean's office has contributed close to $300,000 since 1991 to upgrade the ventilating systems throughout the morphology space and add high quality ceiling-mounted dissecting lamps in the laboratories. These additions are most welcome, not only for safety, but for improved quality of time spent in the laboratories.

Computers in the Classroom

Human morphology at Brown entered the modern technological era with the donation of an Apple Quadra 700 from the Brown Medical School alumni and the purchase of "Animated Dissection of Anatomy for Medicine" software package in 1992. The Animated Dissection of Anatomy for Medicine, or ADAM, is a CD ROM database of male and female anatomy viewed on-screen in anterior, posterior, medial, and lateral perspectives. Students can peel away structures layer by layer or search for specific structures using a find function. While there are many possible uses for ADAM, we have found the most important to be the ability to click on a structure to determine its identity or to use the search function to find a specific structure.

In keeping with our philosophy of providing tools for learning anatomy rather than adding additional components, we've allowed the students to explore the software, on their own, at four workstations. Over the past three years, three major categories of use have emerged:

1) **Preview of dissection.** Students are able to follow the instructions given to them in preparing for the actual dissection. They can preview the incisions, approaches and structures pertinent to each day's material so they are better prepared to grapple with the physical dissection in lab.

> *...we strive to provide an environment in the laboratories which is conducive to the long hours spent either dissecting, studying or interacting.*

2) **Help during lab.** With ADAM, the ability to point and click on a structure to determine its identity can be a tremendous time-saver. Students can rapidly expose structures on the computer rather than flipping through pages of an atlas to locate the appropriate view and identity of a structure. Also, when students are unable to locate a structure in the lab, they can, with a few keystrokes, find the structure on ADAM and determine how to best locate that structure on their cadavers.

3) **Review.** The most widely used feature of ADAM is the idenitification of structures by pointing and clicking with the mouse. Traditional atlases have so many structures labeled that reviewing the material is overwhelming. With ADAM, students are able to quickly review structures to go over a day's dissection or to prepare for an exam. The software also includes cross-sections, CT, and MRI scans for an introduction or review of radiological images.

Plastic Cross-sections

As noted earlier, we believe it to be essential that our first year students are capable of transferring their 3-dimensional view of a dissection to a 2-dimensional image on a viewing box. In 1993, we acquired 25 plastic embedded, cross-sections of a cadaver for use in our laboratory. Each section is labeled (in exquisite detail) and structures are highlighted with muted colored paint. Along with the entire male specimen, we have an additional female pelvis. Prior to sending the entire specimen away to have it prepared, Dr. John Cronan from the Department of Diagnostic Imaging, Rhode Island Hospital, CTscanned the specimen at levels that correspond to the plastic embedded sections. As a result, we have sections of the specimen itself for study and CT scan images at the same level. The CT scan images can be incorporated into the ADAM software, providing another source for review.

Anatomical Gift Program

The dependency of our teaching programs on the generosity of our donors cannot be overstated. Without the

Julie Farley and Win Alford consider an A.D.A.M. image of the head and neck. The A.D.A.M. computer program is a mechanism for review.

willingness of members of the Rhode Island and Massachusetts communities to step forward and commit their physical remains to our educational programs, our ability to teach morphology in the Biomedical facility or at any of the Brown affiliated Hospitals would be greatly impaired.

It is through the Anatomical Gift Program that we acquire the anatomical materials necessary to teach the first-year medical students at Brown, but also to assist in the training of residents in general surgery, neurosurgery, plastic surgery, orthopaedics, obstetrics and gynecology, and emergency medicine. In addition, we serve as a resouce for the University of Rhode Island's Physical Therapy Program. It is important that our clinical and legal communities be aware of our donation program in order to counsel potential subscribers.

Few of us know how to arrange to leave our bodies for anatomical studies. A first step is to request the necessary forms by contacting us at (401) 863-1976. The potenital donor will receive informational material along with the appropriate forms. Once the forms are completed and returned, their bequest will be placed on file in our office. That is all there is to it. When death does occur, all the family has to do is contact us. Our Department takes over, making all the necessary arrangements thereby relieving the family of some of the stress caused by the death of their loved one. Please be alert to potential donors and direct their inquiries to us; their contribution assists us all.

Dr. Wu is an assistant professor in the Department of Ecology and Evolutionary Biology. Dr. Goslow is professor of medical science and vice-chair of the Department of Ecology and Evolutionary Biology.

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Programs Outreach

G.E. Goslow, Jr, PhD

CLINICAL OUTREACH

All of us in the Brown School of Medicine recognize the value of intellectual exchange between our campus-based and hospital-based students (residents) and faculty. Focus around anatomy is a natural and our group has benefitted immensely by helping with some of the hospital-based programs. For six weeks each year for the last four years, we have participated in the Department of Neurosurgery residency-training program at Rhode Island Hospital (RIH). Our limited participation in the Department of Orthopaedics' residency training program has also gone well. In our morphology space at Brown, we have helped the RIH's Department of Emergency Medicine for three years with their two days of "practical anatomy" provided for their residents. In addition, at irregular times, we have shared materials and space for resident-training in Plastic Surgery (RIH), Dermatology (Roger Williams Hospital) and Obstetrics and Gynecology (Women and Infants' Hospital). The common ground of anatomy has not only stimulated teaching, but has fostered some productive research collaborations between us and our hospital-based colleagues

COMMUNITY OUTREACH

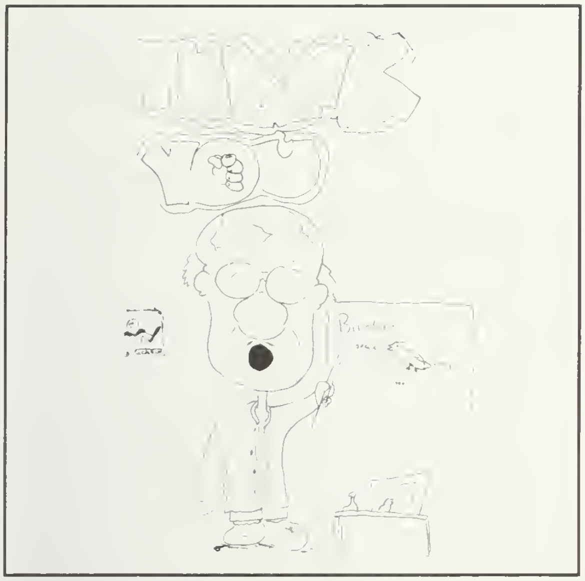
A few days ago, I was explaining to a group of sixth graders how, if they were lucky enough to find a fragment of maxilla or jawbone in a nearby field or vacant lot, they could "read the teeth" to determine whether they had a carnivore, herbivore or omnivore. After going through a few known species, I started hauling out "unknowns." They squealed with delight as they first determined diet and then used that information to make a stab at what the animal might be. The dolphin slowed them down for a few minutes, but once they spotted the nostrils high up on the forehead, they had it. This was at 9:30 am. By 11:00 am, I was trying to help a fourth-year medical student sort out all of the components of the anterior abdominal wall which impinge on direct and indirect hernias and their repair ("just what is the conjoint tendon anyway?"). Both efforts were exhilarating and both are crucial in today's society.

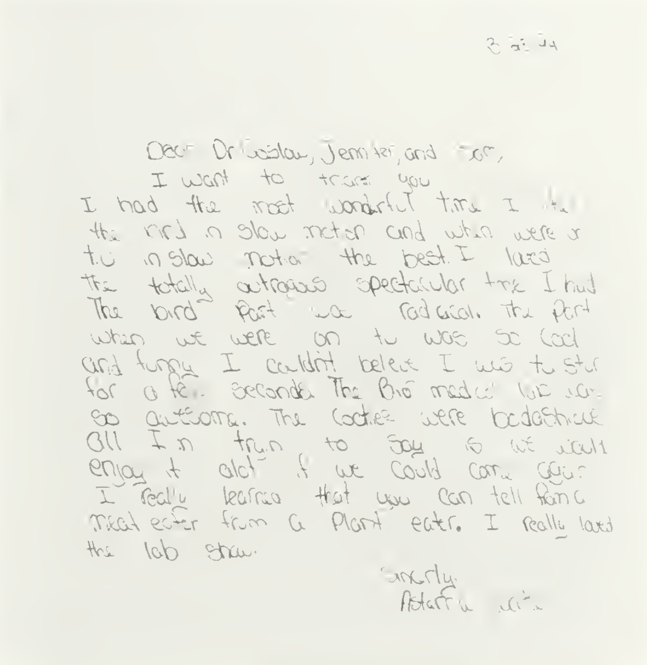
It is cliche to say that we are interested in education at all levels of our community. Nevertheless, we as scientists often get too narrowly focused, begin to take our own research too seriously, and forget that our contributions to education at all levels is not only humane and compassionate, but crucial to the survival of our species. I am not much on bumper stickers, but I do like the one that reads "If you think education is expensive, try ignorance".

The faculty and students within the

Antigone Parker, a senior at Brown, responds to a question asked by a visitor from Mulcahey Intermediate School in Seekonk. As part of an honor's thesis project, Antigone studied the structural/functional properties of the bones in bat wings and here introduces the students to the world of morphometrics.

Jennifer Gray Chickering (left) prepares Sam Poore (right) for a demonstration of electromyography. Jennifer (graduate student) and Sam (technician) illustrate muscle activity patterns visually on the oscilloscope to students from Mulcahey Intermediate School.





3 [illegible] 94

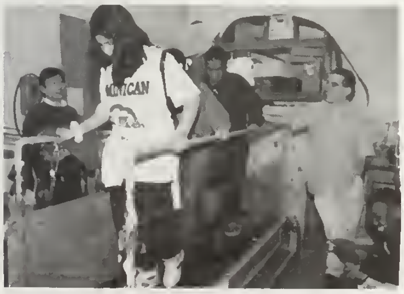
Dear Dr Goslow, Jennifer, and [illegible],
I want to thank you
I had the most wonderful time I [illegible]
the bird in slow motion and when were [illegible]
t.v in slow motion the best. I loved
the totally outrageous spectacular time I had
The bird Part was radical. The part
when we were on tv was so cool
and funny I couldn't beleve I was tv star
for a few seconds. The Bio medical lab was
so awesome. The cookies were bodacious
All I'm trying to say is we would
enjoy it alot if we could come again
I really learned that you can tell from a
meat eater from a Plant eater. I really loved
the lab show.

Sincerly,
[illegible]

Student responses

Department of Ecology and Evolutionary Biology make time, when possible, to reach out to the community schools. Our research spans the gamut of biology from molecular to cellular to organismal to community levels and as such, can be easily demonstrated to visiting classes. The anatomy laboratories have particular interest for advanced high school students studying human biology, surgical technology students from the New England Institute of Technology, and those talented and creative students from the Rhode Island School of Design (RISD) interested in capturing nature through strokes of the brush or pen. Dogs running across a force plate one minute, guinea hens on the treadmill the next. The students seem glued to their seats as they learn how we train these animals and then capture their movements on high-speed video or film. "Awesome" is frequently murmured as a European starling flying in a small wind tunnel easily adjusts to a wind speed increase from 20 to 40 mph in 50 ms. Once sudents understand how we analyze movements, it is easy to engage their attention to illustrate how we measure muscle function through histology and electromyography, determine bone structure by analysis of both its mineral composition and its dynamic patterns of strain during movement, and document the relationships of breathing to stride frequency. During the last year, we provided instructional experiences in morphology for two illustration courses from RISD; Mulcahey Intermediate School, Seekonk; Roger Williams Middle School, Providence; Providence College; The New England Institute of Technology; Burrillville High School, Harrisville; and three groups of National Youth Leadership students.

Amie Valore, a senior at Brown, illustrates the diversity of the shapes of wings found among birds and their functional consequences. Here she moves through a group from Roger Williams Middle School with an eagle wing. Amie's honor's thesis project focused on the organization of muscle for locomotion.



Ernie Wu (left) and Peter Nassar (striped shirt) with students from Roger Williams Middle School introduced them to the somewhat surreal sensation of walking on a treadmill. Students learn first-hand how high-speed video is used to track limb segments in space during walking and running.

> *...we are interested in education at all levels of our community*

Many of our students have contributed to these outreach sessions and several have done so on numerous occasions. We acknowledge the contributions of all but special thanks for considerable help goes to Dr. Ron Meyers, Jennifer Gray Chickering and Don Wilson. The accompanying photos, letters and drawings capture the essence of our outreach and give us pause to smile and realize the two-way affect these encounters have.

Dr. Goslow is professor of medical science and vice-chair of the Department of Ecology and Evolutionary Biology at Brown University

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Research in Morphology at Brown

Evolution of the Axial Musculoskeletal System

Dale Ritter, Graduate Student

When people visit our laboratories or are likewise briefly exposed to our research in progress, many go away wondering why anyone would want to know when a particular muscle is active, or when the angle formed by a particular body part reaches a maximum value. People see us gathering data that addresses very specific questions, and more often than not, they are not introduced to the broader questions we are pursuing. Outside the context of these broad questions, the work we do on a daily basis can appear quite esoteric. I have been asked to provide a general context for the collective statements of research that follow. I want to convey a sense of the types of broad questions that we, as morphologists in the Department of Ecology and Evolutionary Biology, find interesting and worth pursuing, as well as a general sense of how that pursuit occurs. As an example, I will use the research I have been involved with at Brown as part of my dissertation. I will start by introducing the very broad question that I am pursuing, identify the sub-sub-disciplines of biological science under which one may accurately file the research I do, outline how a research project such as mine may develop, and then end with some general results of my research, and its broad implications.

In very general terms, I am interested in the locomotor function of the axial musculoskeletal system, and the evolution of that function in vertebrate animals. That is, what does the trunk do during locomotion in vertebrates, and what are the changes that have occurred in the axial system during the evolution of vertebrate animals? Although easy to forget from our human viewpoint, the trunk plays a vital role in powering locomotion in the majority of vertebrate animals. This is evident in the swimming of most fishes as well as in the terrestrial locomotion of animals such as snakes. Many mammals employ their trunks to some degree during locomotion as well. For example, it has been estimated that a sprinting cheetah augments its speed by 6 miles per hour due to the flexion and extension of its back[1]. In another major group of vertebrates, birds, elements of the vertebral column have undergone substantial fusion, resulting in a trunk that is basically a stiff rod of bone. This stiff trunk is believed to provide a solid base for the muscles that oscillate the wings during flight. So we see that movements of the trunk may be the sole engine of locomotion (as in many fishes and all snakes), locomotion may be accompanied by minimal movements of the trunk (birds), or the contribution of the trunk may be somewhere between these two extremes (galloping mammals). In all cases, the trunk is vital to effective locomotion.

> *Functional morphologists are particularly interested in how organisms work, while evolutionary biologists are interested in how organisms change through time.*

The approach I have taken in attempting to address locomotor function of the axial musculoskeletal system defines the "type" of research I do. I am most comfortable calling myself a functional morphologist with strong interests in evolutionary biology. Functional morphologists are particularly interested in how organisms work, while evolutionary biologists are interested in how organisms change through time. I am interested in vertebrate animals. Therefore, I may fully describe my scientific interests as encompassing vertebrate evolutionary functional morphology; I investigate how animals work, and how the way they work has changed during evolution. I believe this research approach works well with the broad question I am investigating. As a functional morphologist, I am continually amazed at the myriad ways the trunk is employed by animals during locomotion, and at the concomitant morphological and functional specializations evident in the various groups of vertebrates. As an evolutionary biologist, I am intrigued by attempts to reconstruct the functional history of the trunk. The disciplines of functional morphology and evolutionary biology are intimately linked. Knowing the history of both the organisms and the functional systems we investigate guides us in asking relevant questions. Likewise, the answers gained from functional studies increase our knowledge of evolutionary history and its mechanisms.

Given a broad question and research approach, a particular organism or group of organisms exist which are the most appropriate experimental subjects. From both a functional and an evolutionary perspective, lizards are a key group for studies of axial locomotion because in many respects they represent an intermediate condition between basal, or "primitive" vertebrates (fish and amphibians), and derived vertebrates (mammals and birds). After identifying the most appropriate group of animals to concentrate my research efforts on, I must begin to narrow the very broad question of axial musculoskeletal function into smaller, more "answerable" questions. An initial specific question might be, why do lizards bend laterally during locomotion? The probable answer to this question is that lizards "inherited" lateral bending from more basal vertebrates. A second, more specific question, might follow, what does lateral bending accomplish for lizards? Other vertebrates that bend laterally do so in order to swim (fish and amphibians). The vast majority of lizards, however, are completely terrestrial animals, so that the function of lateral bending is not obvious. This process of asking increasingly specific questions continues until we have a set of questions that may be addressed by acquiring data from animals.

Just as question asking proceeds from general to specific, so may the data acquisition process. We may film or

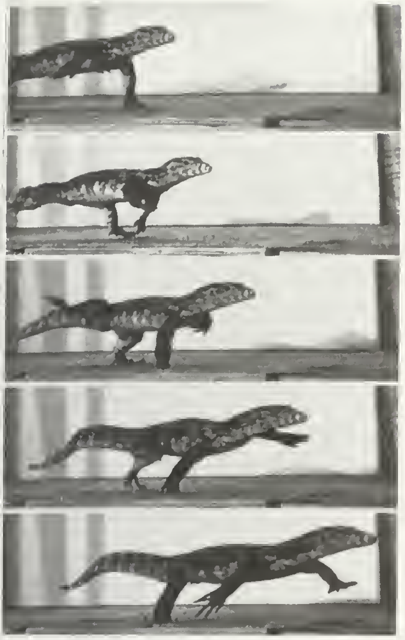

Figure 1. Video frames of a water monitor (*Varanus salvator*) running at a speed of 4 meters/second. The time between consecutive video frames is 32 milliseconds (0.032 seconds). In several aspects of their locomotion, lizards exhibit characteristics of both advanced vertebrates (mammals) and more basal vertebrates (amphibians). For example, lizards are capable of attaining the same maximum speed as similar-sized mammals, but retain the sprawled limb posture and lateral trunk bending of their amphibian ancestors.

videotape animals as they move, in order to quantify their trunk movements. These kinematic analyses allow comparisons that are both general (primitive vertebrates bend their trunks laterally, while more derived vertebrates bend sagitally, or not at all), as well as finer-scale comparisons. For example, although lizards and salamanders both bend laterally during terrestrial locomotion, we may ask whether they bend the same amount, whether they bend in the same regions of the trunk, or how bending changes with speed? Once we have quantified the movements, we may embark on attempts to determine how these movements are produced. We begin with a thorough analysis of the animal's anatomy; what muscles are in the appropriate location and exhibit the appropriate orientation to make them likely candidates for further study? After identifying promising muscles, an electromyographic study may be done. This involves recording the electrical activity of muscles during locomotion (or any other behavior one is interested in) to determine if the muscles are active at an appropriate time to produce the observed movements. Using these and other tools (e.g. muscle stimulation procedures, denervation experiments) we are eventually able to formulate hypotheses about the function of the movements we observe, as well as what muscles produce those movements.

What have we learned about the function of lizard trunks, and what may this tell us about the evolution of the locomotor function of vertebrate trunks in general? Lizards and salamanders are similar in that they both bend laterally during locomotion, but there the similarities end. Salamanders show the greatest amplitude of bending at the level of their pectoral and pelvic girdles, and the amplitude of bending increases with increasing speed. Lizards show the greatest amplitude of bending midway between the pectoral and pelvic girdle, and the amplitude of bending decreases with increased speed. Salamanders use their epaxial muscles to produce lateral bending of the trunk[2], but it appears that lizards do not. In fact, I have proposed that lizards use their epaxial muscles as postural muscles during locomotion; that is, the epaxial muscles of lizards appear to function in reducing, rather than producing, movements of the trunk[3] (Fig. 1). This hypothesized postural function for the epaxial muscles of lizards is similar to the proposed function of the epaxial muscles of mammals. In evolutionary terms, what we currently know indicates that as vertebrates moved to land, lateral bending of the trunk was of reduced importance, and may in some aspects be a hindrance to terrestrial locomotion. This is not surprising, as lateral bending was originally employed for swimming. The move to land also placed greater importance on an organism's ability to counteract the force of gravity. The use of the epaxial muscles in a postural role may have been an important innovation among vertebrates, allowing them enhanced terrestrial locomotor performance. Hypotheses generated from this and other studies of lizard locomotion allow us to make predictions about axial musculoskeletal function in other vertebrates, thereby suggesting future research projects. In many aspects, our research projects may be said to take on a life of their own, effectively pointing out the next most logical step of an investigation

"Doing" research is a dynamic, multifaceted process, which I have portrayed here as unrealistically linear. As we integrate the data we and our colleagues collect into what is "known" about a particular subject, we constantly re-evaluate the questions we ask, the methods we use, and the organisms we study. Our goal is to derive general statements about organismal function, so that ultimately we may better understand the great diversity of life. These general statements come from research at all levels of integration, from the interactions of sub-atomic particles to the interactions of the plants and animals in an ecosystem. In all cases, general statements result from a great deal of specific investigation, often by several generations of scientists working in diverse disciplines. All levels of analysis are necessary, all are informative. As morphologists we generally work at the level of the whole organism, although we alternately sharpen and broaden our focus as a developing project dictates.

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Evolution of Specialization

Katherine D. Earls, Graduate Student

The broad context of my research concerns the evolution of specialization, with a focus on the factors that limit locomotor performance in birds. Birds exhibit a varied array of specializations in lifestyle and behavior. These are associated with a large diversity of body forms, from man-sized, obligate bipeds (ratites) to insect-sized, specialized hovercraft (hummingbirds). My current project centers around the observation that, among these specialized forms, we seldom see birds which are equally adept at flight and terrestrial locomotion. It is true that some birds, small shorebirds (e.g. sandpipers, plovers) for example, are excellent fliers capable of covering long distances as well as maneuvering in close spaces. They also spend significant time on the ground, running while foraging. In contrast, both locomotor abilities are not evident in their larger shorebird cousins (e.g. yellow legs, curlews), which are quite capable of the same type of flight but, when moving around on the ground, they tend to walk slowly and prefer to fly from place to place, rather than run. This observation indicates that size, combined with general body type, could be a limitation on locomotor performance. Size itself is unlikely be the sole limiting factor as many birds get quite large, so there may be some interaction between body size and shape which determines locomotor capabilities. What are these interactions, and how do they relate to the evolution and specialization of birds?

There are a variety of ways one might address this question. For example, clues may emerge from studies of ecology, physiology, or behavior of birds with unique specializations. I decided to combine my background in anatomy and engineering, and pursue the hypothesis that there are mechanical tradeoffs which have been imposed on birds by their evolution. Powered flight and ground locomotion, while involving different limbs, have competing requirements for optimal performance. Legs need to be strong and muscular for sustained running or walking, but overall the body needs to be light for speed and maneuverability in the air. I have started a series of experiments which will define the specific nature of these tradeoffs and provide information about the range of abilities of differentially specialized birds.

I have begun by making use of the ornithology collections at the Peabody Museum at Yale, and the Museum of Comparative Zoology at Harvard. By measuring x-ray images of the limb bones of terrestrially and aerially specialized birds, I am able to quantify and define shape differences. It has been assumed that terrestrially specialized forms have longer legs, and that their wings are reduced compared to aerial specialists. Preliminary analysis, however, shows that terrestrial specialists have the same range of hindlimb lengths as non-terrestrial forms. Wings of terrestrial birds are short, but they are also reduced in strength, and may be unable to resist the same forces as aerially specialized forms (Figs. 2 and 3).

Over the next couple of years, I will bring the results of this skeletal analysis into the laboratory, measuring the kinematics of locomotion in terrestrial and non terrestrial birds. Quite a bit of data has been collected about the mechanics of bird flight but, due to structural differences, the flight of terrestrial birds can be expected to be different from that of species studied (e.g. pigeons, starlings). With shorter, weaker wings and heavier hindlimbs, terrestrial birds should takeoff and fly differently from non-terrestrial birds. They should also be capable of higher speeds on the ground.

I am beginning to test these hypotheses by training birds to take off from a small force plate, and fly to a predetermined perch. In this way, I can record

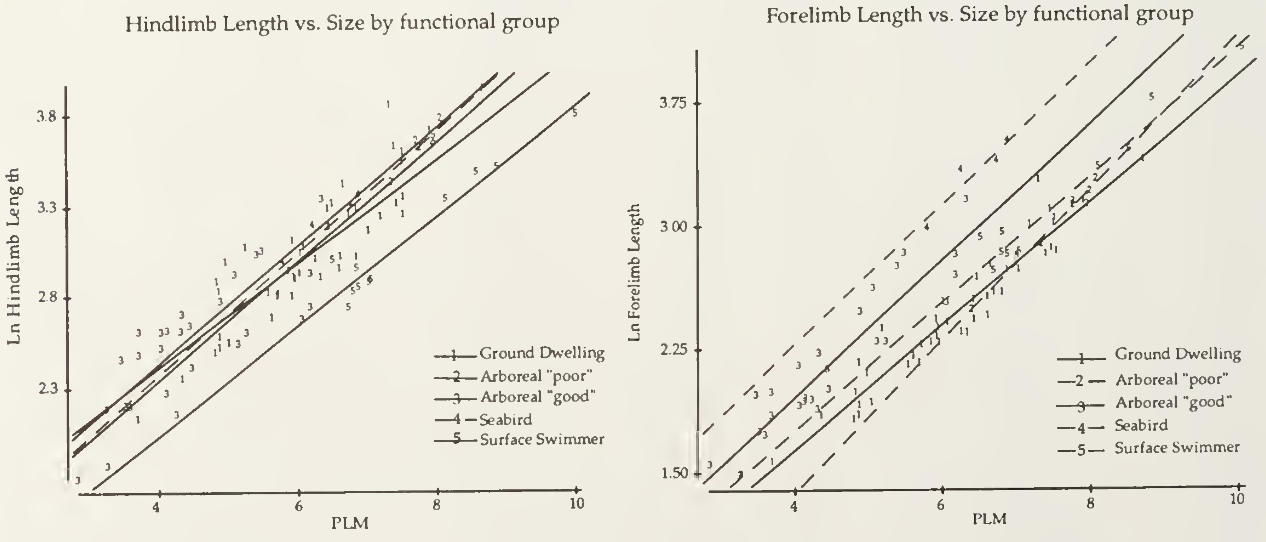
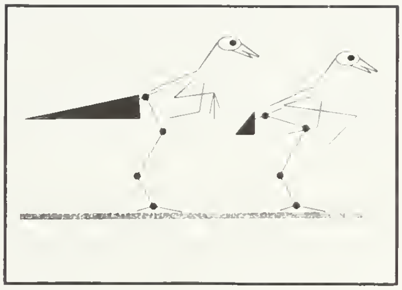


Figure 2. When bone length data are analyzed by functional group, the patterns reveal potential functional differences. Counter to predictions based on cursoriality theory, only surface swimming birds have hindlimbs which are different in length than other groups (left). Cursoriality arguments predict that ground dwellers should have longer legs than nonground dwellers, but these data show that ground dwellers have the same limb lengths as more aerial specialists. Forelimb length data (right), follow predictions based on flight ability, with the more specialized fliers, the seabirds and arboreal "good," possessing the longest wings.

Figure 3. Present day birds have much shorter tails than did their ancestors, the tail vertebrae being reduced to a pygostyle which supports the tail feathers. The loss of the heavy, muscular tail (left) caused the center of gravity to shift forward. This forward shift necessitated a reorientation of the hindlimb (right), fixing the femur in a nearly horizontal position. Any further changes in position of the center of mass, with increase or decrease in flight musculature may cause changes in the mechanics of how the avian hindlimb is used.



the force which the bird produces against the ground, and make video and/or cinematographic recordings of the takeoff. Comparing the wingbeats, body position, and ground reaction forces of terrestrial and non-terrestrial birds of the same size will give me specific data about what is different in their flight. Finally, I will perform the same types of experiments with the birds walking and running over the force plate.

The data I collect from these experiments, combined with the skeletal information collected from museum specimens, will give us a clearer picture of the locomotion of birds in general. Understanding the locomotion of living birds gives us a way to look at the evolutionary past of birds as they arose from theropod dinosaurs and to predict the types of constraints which may have channeled the evolution of powered flight.

The Effect of Musculoskeletal Morphology and Body Size on Locomotor Function

Jennifer Gray Chickering, PhD, Recent Graduate

When asked to write a short article about my motivation and interests as a scientist, I began, as a true evolutionary biologist, to reflect on history...my history. I now realize that the third grade was a fundamental and pivatol point in my career. Fundamental in two ways: 1) in third grade we wrote and compiled reports on animals, a project which culminated in an impression-making field trip to the zoo and 2), upon realizing that I really liked science class, at eight years old I decided I wanted to be a doctor. Young but motivated I decided to immediately get started on my medical education. The school librarian somewhat reluctantly allowed me to venture into the "big" kids library to check out a book entitled *The Human Body*. In a week I could name all Eight Systems of the human body as well as tell you the number of bones in the human body – I could even name quite a few (those carpal bones still give me problems). I even learned about a few processes I hadn't quite heard about yet (Ch. 8 Human Reproduction). The pivotal part of third grade hinges on a purchase I made later that year at a used book sale – *Human Pathology* for 25¢. After perusing the photos in that book, I had thoroughly freaked myself out and decided then that I no longer wanted to be a doctor!

I maintained my fascination with animals, however, which was borne out over the years primarily through small pet ownership: mice, fish, newts, parakeet, etc. It really wasn't until college that my interest in biology and, more specifically, in animal form was once again peaked. The concept of evolution and the study of morphology, first introduced in my core biology class and brought together in my comparative vertebrate morphology class, were IT. The evolutionary framework and its explanatory stories made sense of the wide variety of animal structures we studied. This time around, I found out about research and graduate school.

I entered the Brown graduate program in Ecology and Evolutionary Biology in 1990 with an interest in vertebrate morphology and locomotion. Although my approach has been refined as I have developed expertise during my graduate education, it is still these primary curiosities that shape my research, and it is the same third grade wonder of animals that drives me. More specifically, I am interested in the effect of musculoskeletal morphology and body size on locomotor function, and the evolution of constraints and adaptations in these systems. Currently, I am studying these topics in a common taxon of mammals: squirrels (Family Sciuridae of the Order Rodentia). The evolution of morphology is summarized in figure 4: a circle of one-way but continuous influence linking morphology, performance, and fitness[4]. Performance is basically the functional aspect of morphological features and the arrow of influence between the two reflects the effect that variation in morphology has on function. An example, two birds, the morphological variate: one has a longer bill, the function: feeding, the consequence: the longer-billed bird has enhanced performance reaching insects in holes and crevices in trees. Fitness is the number of reproductively successful offspring an organism leaves, i.e., the more copies of your genes that you contribute to a population relative to others, the more fit you are. The arrow of influence linking performance and fitness reflects the effect that variation in performance has on fitness. Thus, the bill morphology that affected feeding performance only matters evolutionarily if that enhanced performance allows the longer-billed bird to reproduce more longer-billed, performance enhanced offspring, perhaps by feeding more or more efficiently. The link between fitness and morphology sums up the story; those morphology/performance complexes that are more fit will survive. If the shorter-billed bird does not successfully reproduce, the short bill morphology will disappear.

I am interested in the causal link between morphology and performance and in particular, how the variation in

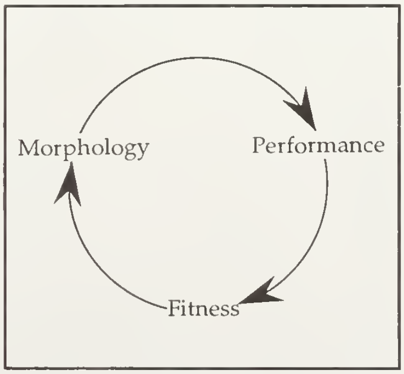


Figure 4. The Evolution of Morphology. Depiction of the circle of one-way but continuous influence linking morphology, performance and fitness. (After Arnold, 1983).

morphology of bones and muscles among species of squirrels relates to differences in sprint performance, an ecologically relevent locomotor function. To investigate this, I have obtained wild squirrels in cooperation with professors and students at Northern Arizona University, and forest service scientists in South Carolina, and local pest controllers. I collect performance data from the squirrels by inducing them to sprint through an enclosed trackway while videotaping. To further sort out performance, I have squirrels run on "branches" (mesh-covered PVC pipe) of varying diameters and on a flat board. Variables such as speed, stride length, stride frequency, and measures of stability are quantified from videotapes via computer motion-analysis software. These performance parameters are then analyzed to determine how they vary with body mass, morphology, and natural habitat preferences among squirrels. Hypotheses based on morphological variation coupled with biomechanical models can be formally tested.

In a nutshell (get it?), I have found that gliding squirrels are slower on both branches and flat surfaces than all other squirrels, including the chipmunk, a squirrel of similar bodysize. Flying squirrels have relatively longer limbs than both arboreal (climbing) and terrestrial squirrels; increased limb length may impede sprinting ability on branches: if your limbs are longer, your center of mass is further from the branch and it is presumably more difficult to balance while sprinting. In addition, the wing membrane of flying squirrels may impede running ability (Fig. 5). Arboreal species are less sensitive to changes in branch diameter than are the terrestrial or gliding species. This result reflects the natural habitat usage of these species-only arboreal squirrels regularly travel distances through the tree canopy. Larger arboreal squirrels, who may be predicted to have difficulty on very small branches and might slow their speed, seem instead to switch their mode of running from one based on static control (carefully balancing) to one based on dynamic control (relying on forward momentum to traverse the distance). However, dynamic control has its costs – squirrels are more likely to fall, but if balancing over a small diameter branch is impossible, an arboreal squirrel may simply take its chances in the face of danger. In both the flying squirrel and the chipmunk, speed decreases with decreasing branch diameter, a result in keeping with the natural habitat preference of these species. Within arboreal squirrels, I can address the affect of body size on sprint speed. In general, sprint speed is independent of mass in arboreal squirrels ranging from ~200 g to over 700 g. This result provides some of the first evidence for hypotheses initially proposed in 1950 by a famous (at least in our circles) physiologist named A.V. Hill[5,6].

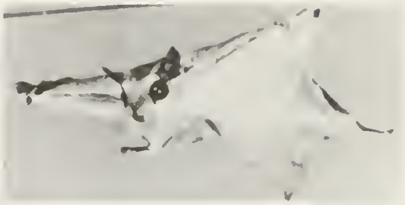


Figure 5. The flying squirrel (Glaucomys) in its 'gliding' posture. Although the wing membrane clearly enhances the animal's ability to extend the distance traveled when leaping from one branch to another, the membrane may impede running performance on the ground. (From Nowak's Walker's Mammals of the World [5th edition]).

The next step is to correlate morphological variation among squirrels with these differences in sprint performance. There are many possible morphological determinants of sprint speed and I have chosen a subset for analyses in three species of squirrels. These include shape and scaling in hind and forelimb bones,[7] mass, fiber angle, and fiber length in 15 limb muscles, and fiber type profiles and fiber areas in three key locomotor muscles. Investigation of these parameters and how they relate to documented performance variation will not only address the influential link between morphology and performance, but will also provide us with information about what types of morphology vary among closely related mammalian species. This knowledge will help us understand the possible patterns of morphological change which can occur during evolution, and provide insight into adaptation and constraint in locomotor morphology function complexes.

Although the work outlined above represents my Ph.D. dissertation research, I have also been involved in other research at Brown. In collaboration with Dr. Alan Sokoloff and Dr. Jason Harry, an engineering professor, and under the guidance of Dr. Ted Goslow, we investigated the evolutionary and functional significance of a novel wing-elevator muscle in birds. In a series of experiments with European starlings and pigeons, we monitored electromyograms of this wing-elevator muscle and wing kinematics during takeoff and flight. We then either cut the insertion tendon of the muscle or severed the nerve to the muscle and subsequently monitored muscle activity (or lack thereof) and wing kinematics. This work coupled with ongoing work in Dr. Goslow's lab, has provided valuable insight into the locomotor function of this muscle as well as headway into the age-old, but still unanswered question, How do birds fly[8]?

As a side project to my work with squirrels and in collaboration with Dr. Sokoloff, I investigated the innervation pattern of novel musculature associated with the wing membrane in flying squirrels. Using retrograde nerve tracing techniques we documented an unusual pattern of dual innervation in this flight muscle: motor innervation from both cranial and cervical spinal sources. This pattern when compared with similar patterns found in other,unrelated flying and gliding mammals indicated a convergent evolution of wing morphology among flighted mammals[9].

Finally, I was lucky enough to travel to Australia to take part in a project directed by my advisor, Dr. Sharon Swartz and in collaboration with an Australian colleague, Dr. Mike Bennett, and a Brown undergraduate, Antigone Parker. We investigated the patterns of bone strain in free-flying Australian fruit bats. These bats (with wing spans up to 6 feet) are large enough to allow surgical implantation of miniature strain gauges on wing bones. By simultaneously recording bone strain and videotaping flight sequences, strain patterns can be correlated with wing movements. We found patterns of torsional loading in wing bones which can be related to the architecture of these bones; in addition, we found the highest strains ever recorded in mammalian bone in distal elements (proximal phalanges) of the bat wing[10].

There are so many interesting questions to be asked in evolutionary morphology, all of them exciting and important. One future direction of particular interest to me is addressing gestation as a contraint during the evolution of mammals. I hope to address this by studying the morphological and performance effects of gestation by comparing animals of different phylogeny, body size and locomotor life history. Gestation is an often overlooked part of life history which is obviously and directly related to evolutionary fitness. The ability to escape predators, for instance, is difficult – we've all seen unsuccessful escape attempts in nature or through film – how much more difficult might escape be during gestation? Are there specific adaptations either morphologic, physiologic, or reproductive which balance detrimental effects on locomotion? And how might such adaptations in turn constrain the evolution of mammals, both male and female?

I want to wrap up this essay by reflecting once again on third grade to point out something that has only more recently become fundamental to my career goals. The reason third grade made such an impact on my life was because of the outstanding educators that I encountered that year. Mrs. Kisabeth, my third grade teacher, and Miss Betty, the librarian whose last name I never knew, recognized my excitement, encouraged and facilitated my seeking a higher level of knowledge – even at that young age cultivating my intellect. Drs. Alan Jaslow and Carolyn Jaslow, professors at Rhodes College, were the next to encourage my intellectual growth. As my major advisor, Alan Jaslow was enthusiastic about my interest in biology, helped me obtain a research internship, guided my ongoing research and was fundamental in my decision to apply for a position in a graduate program. Both of the Drs. Jaslow were supportive and inspired teachers and were committed enough to have literature discussions in their home for another student and myself. Graduate school has been the first opportunity I've had to teach students, and success in teaching has now become a very important goal for me. The desire to teach and teach well is also selfishly motivated – being able to turn on a light in a student's mind with thought-provoking questions, successfully clearing up a fog of confusion about gut development and exactly which mesentery is which, prodding students to figure out an answer for themselves instead of just telling them, and seeing interest in subjects I love grow in the students I teach – these are true pleasures and bring fufillment I will always enjoy. My commitment to education and the realization of the impact an educator can have in the lives of his or her students has been further fuelled by my experiences of learning from and teaching with Dr. Ted Goslow, Dr. Sharon Swartz, Dr. Dave Carrier, and Dr. Christine Janis at Brown.

I would like to end with a note of advice for all doctors: Beware in whose hands your old Human Pathology text falls!

How Terrestrial Vertebrates Breathe When They Walk and Run

David R. Carrier, PhD,
Assistant Professor of Biology

The primary focus of my research is concerned with how terrestrial vertebrates breathe when they walk and run. For an animal to sustain vigorous locomotion it must continue to breathe as it runs. When mammals run they take one complete breath during each cycle of limb movement. Imagine a greyhound galloping. As the hound lands on its front limbs and curls its back to swing the hind limbs under the body, the volume of the thoracic cavity is compressed and air is pumped out of the lungs. Hind feet then contact the ground and the hound accelerates forward, straightening its back, which expands the volume of the thoracic cavity and simultaneously sucks air into the lungs. Thus, the muscles and bones of the thorax are instrumental in producing both locomotion and ventilation. For both to happen simultaneously they must be synchronized. However, locomotor and ventilatory actions of the trunk muscles are not always compatible.

Lizards are a group in which there is a conflict. Based on their musculo-skeletal anatomy and mode of locomotion, I postulated that lizards would not be able to run and breathe simultaneously. The same muscles which bend the trunk from side to side during running seemed also to be responsible for breathing, making simultaneous running and breathing impossible (Fig. 6). To test this, I measured lung ventilation in several species of lizard as they walked and ran on a track[11]. Demonstration of significant ventilation during locomotion would have refuted the hypothesis. However, in all the animals tested, ventilation dropped off as running speed increased. To determine if a mechanical constraint was responsible, I analyzed the activity of the trunk muscles during both lung ventilation and walking in one species of lizard, green iguanas. In this species, the four muscles involved in breathing were also active during locomotion, and their activity conflicted with the movements necessary for breathing. Thus, lizards are not able to run and breathe at the same time.

Based on information from the fossil record, I have suggested that, like lizards, primitive terrestrial vertebrates

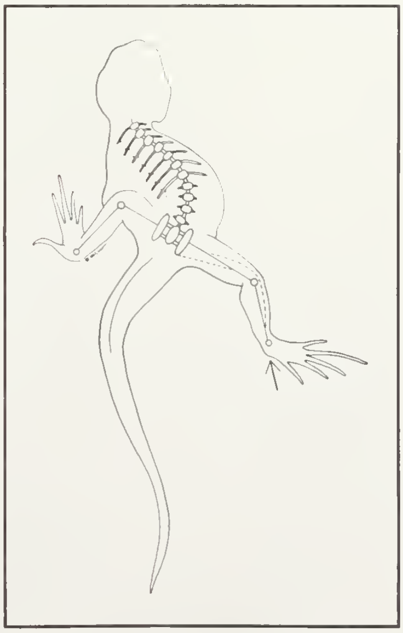


Figure 6. Schematic representation of relevant skeletal and muscular elements in a lizard running bipedally. During locomotion the muscles (dashed lines) of the thorax are expected to contract unilaterally, first on one side and then on the other during each locomotor cycle. Such unilateral contraction elicits lateral bending of the trunk and stabilizes the pelvis against forces applied by the appendicular muscles. In this example, propulsive force applied to the ground (arrow) by the right hind limb exerts a counter-clockwise rotational torque on the pelvis. Axial musculature of the left side contracts to anchor the pelvis. Unilateral activation of the thoracic musculature is suggested to be incompatible with effective aspiration breathing. Modified from Snyder (1962). (After Carrier, 1987)[11].

may have been unable to breathe during locomotor activity. Such a constraint in the early tetrapods would have had a dramatic effect on subsequent evolution. On the one hand, an initial constraint on simultaneous running and breathing may have been one of the factors that directed the ancestors of lizards towards specialization in burst activity based on anaerobic metabolism. On the other hand, the lineages from which birds and mammals are derived seem to have undergone anatomical changes, such as the adoption of upright posture and diaphragmatic muscles, that enable simultaneous running and breathing. Such changes from the ancestral condition would have been prerequisite to the evolution of a capacity for sustained locomotion.

My lab is continuing to investigate the role of the trunk muscles in locomotion and ventilation. Biologists now have a good understanding of the role that the muscles and bones of the trunk play in lung ventilation in stationary subjects. Indeed, these muscles are generally thought of as ventilatory muscles. However, recent observations suggest that these muscles are primarily organized for locomotion. We are addressing the hypothesis that the basic organization of the axial musculoskeletal system is a direct reflection of the locomotor role[12]. To sort out what the muscles of the trunk do during locomotion, we are measuring the activity of the axial muscles in running lizards and mammals and correlating that activity with bending of the trunk, forces exerted against the ground by the limbs, strain induced in the ribs and ventilatory air flow (Fig. 7). Work is also ongoing on three related projects: locomotor ventilatory coupling in running birds, integration of locomotor and cardiac rhythms in running dogs, and venous return and cardiac output in running lizards.

A second topic I am very interested in is the postnatal/posthatching ontogeny of the locomotor system. Young animals must often maneuver in the same environment and face the same predators and prey as adults. Yet, they do this at a time when the tissues of their locomotor system are rapidly growing and differentiating. Work that I have done on Black tailed Jackrabbits and California Gulls suggests that the requirements of postnatal ontogeny are not always compatible with locomotor function[13,14]. There are two broad questions which I plan to pursue in the future. 1) To what extent does selection on the locomotor performance of juveniles influence the phenotype of adults? Because juveniles are often subjected to greater rates of predation than adults, there will, in many species, be strong selection on the locomotor performance of juveniles. In those species, the adult configuration may be determined more by the extent to which ontogenetic pathways can respond to selection on juveniles than to direct selection on the adult phenotype. This is a question that can be addressed via selection experiments, possibly with mice. 2) What influence does physical activity (i.e., exercise) during growth and development have on the configuration of the adult phenotype? Some information relevant to this question is available, but the issue has not been addressed in a thorough manner. A tantalizing observation comes from a comparison of children who grow up at high versus low altitude in the Andes Mountains. Those who mature at high elevations tend to have broader chests and presumably larger lungs than those who grow up at sea level. I am hoping to begin experiments on the effect of exercise during growth in the near future.

A third project my lab is investigating is the possibility that running animals may have the ability to change the gear ratio of their limb muscles. Skeletal muscles have a narrow range of shortening velocities at which they can generate high power. In this sense they are analogous to the internal combustion engines of automobiles. In car engines there is a rate of piston revolution at which power is maximized. When we accelerate from a stop in a car, we start off in low gear and increase speed by increasing the rate of piston revolution. However, we quickly reach a speed at which further increases in piston turn over results in a loss of power and a decrease in the ability to accelerate. At this point we shift to a higher gear. The transmission of a car makes it possible to maintain high power over a range of ground speeds. Variable gearing in the musculoskeletal system of animals would be advantageous for much the same reason. We suspect that toes may make variable gearing possible around the ankle joint[15]. The idea is that during the course of a step the center of pressure under the foot translates forward. On landing the center of pressure is located under the heal. It shifts forward under the foot as the step progresses and is under the tips of the toes at takeoff. This translation could, in theory, increase the length of the out lever of the ankle, thereby increasing the gear ratio. Recordings we have make in running humans indicate that the gear ratio of the ankle does change in the predicted manner. We plan to do further experiments in jumping frogs.

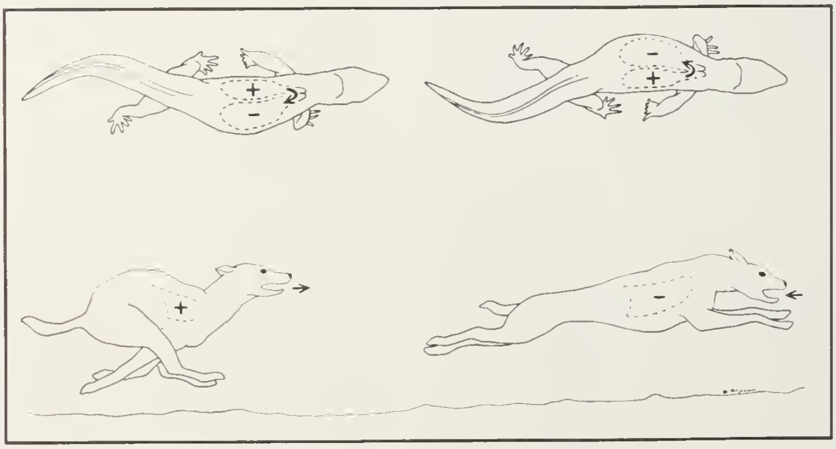


Figure 7. Comparison of the effect that axial bending has on lung volume in a running lizard and a galloping dog. In the case of the lizard, the bending axis of the thorax is situated between the right and left lobes of the lungs. As the lizard bends laterally to one side, one lobe is expected to experience a reduction in volume while the other expands. Air may be pumped (indicated by arrows) back and forth between the lungs, but little if any will be moved in and out of the animal. In contrast, the bending axis of a galloping mammal is dorsal to the thoracic cavity. Sagittal bending changes the thoracic volume and actively pumps air in and out of the lungs during each locomotor cycle. (The dog is modified from Muybridge, 1887.) (After Carrier, 1987)[11].

Evolution and Paleobiology of Vertebrates

Christine Janis, PhD, Associate Professor of Biology

My interests are in the evolution and paleobiology of vertebrates, primarily hoofed mammals (ungulates), but I maintain interests in, and occasionally have published upon, a wide range of topics in vertebrate evolution.

My research falls into two main areas (a third, more minor one, is in the systematics of ruminant artiodactyls):

1) The correlation between skeletal morphology and behavior, and in using the correlations derived from the living animals to determine the probable behavior of extinct taxa. My initial interest was in the craniodental morphology and feeding behavior in herbivores,[16] but I have become increasingly interested in the evolution of cursorial locomotion in mammals in general.[17,18]

2) Patterns of Cenozoic mammalian faunal change and community evolution in relation to changing vegetation and climate. I am especially interested in the evolution of the Miocene savanna ecosystem in North America. For the past several years I have been amassing data on Tertiary mammal faunal assemblages, in correlation with my editorial work on a multiauthored book: *Evolution of Tertiary Mammals of North America*. I plan to incorporate these data into a computerized data base that will be available to other workers. I am currently planning a collaboration with European researchers on a comparison of evolutionary patterns between North American and Old World Neogene mammal faunas.

These two apparently disparate areas can be related to each other as follows. An understanding of the diversity of feeding and locomotor behaviors (plus range of body sizes) in a mammalian assemblage (living or fossil) is reflective of the structure of the habitat. It is usually held that "The Present is the Key to the Past": yet I am becoming increasingly interested in the possibility of both subtle and more radical differences in even relatively recent (Neogene) habitats and ecosystems in comparison with those of the present day. For example, the mammalian communities of the supposed savannas of the late Miocene of North America have certain ecomorphological differences to those of present day East African savannas (absence of pursuit predators, large diversity of grazing horses but no grazing ruminants) that may indicate a precise type of habitat unknown today.

Factors Dictating Variations in the Performance of the Skeleton

Sharon Swartz, PhD, Assistant Professor of Medical Science and Engineering

"Morphology . . . is the most interesting department of natural history, and may be said to be its very soul. What can be more curious than that the hand of a man, formed for grasping, that of a mole for digging, the leg of the horse, the paddle of the porpoise, and the wing of the bat, should all be constructed on the same pattern, and should include the same bones, in the same relative positions?"

Charles Darwin
On the Origin of Species by Means of Natural Selection, 1859

Biologists have been fascinated by the structural design of the skeleton for centuries, and have sought to understand both the unity of design among related creatures and the adaptation of design to specific functions since at least the onset of the Darwinian revolution. Like Darwin, I find myself captivated by the patterns of architectural similarity among mammalian limbs, and like many morphologists both before and after Darwin's day, I am drawn to try to explain the differences in anatomical construction among animals that put their bodies to different kinds of uses. So, my research program seeks to understand the functional significance of the morphological variation in musculoskeletal design among species, and to use functional and biomechanical understanding to gain new insights into evolutionary history.

Morphological features, particularly skeletal features, often show patterns of diversity among taxa that are correlated with corresponding patterns of functional capabilities. By rigorous analysis of these complex structure/function interrelationships I believe we gain understanding both of the adaptation of form and function to the environment and of the nature of evolutionary changes in morphology and behavior. Therefore, my primary areas of inquiry are:

1) to identify and explain those factors dictating musculoskeletal design in mammals, and in particular, to investigate the relationship between bone size and shape and mechanical loading imposed by locomotion;

2) to apply these results to the analysis of patterns of morphological change and phylogenetic diversification within mammals.

One example of my research using this approach concerns the relationship between skeletal design and the mechanics of support in the forelimb of suspensory primates. In suspensory species, particularly the gibbons, small-bodied apes that move through the rain forest canopy by swinging by their forelimbs, the mechanical "environment" imposed on the skeleton by locomotor behavior is fundamentally different from that experienced by their non-suspensory relatives. In these animals, the limb as a whole bears predominantly tensile rather than bending and compressive loads. I used principles of mechanical design to develop a series of testable hypotheses about the specific ways in which the limb morphology and biomechanical scaling of suspensory species should differ from those of related non-suspensory species. I tested these hypotheses by a comparative study of biomechanically critical morphological features among related suspensory and non-suspensory taxa.

Simultaneously, I have borrowed a technique used widely among mechanical engineers to pursue a direct and in-depth analysis of the pattern of bone loading of suspensory primates during a

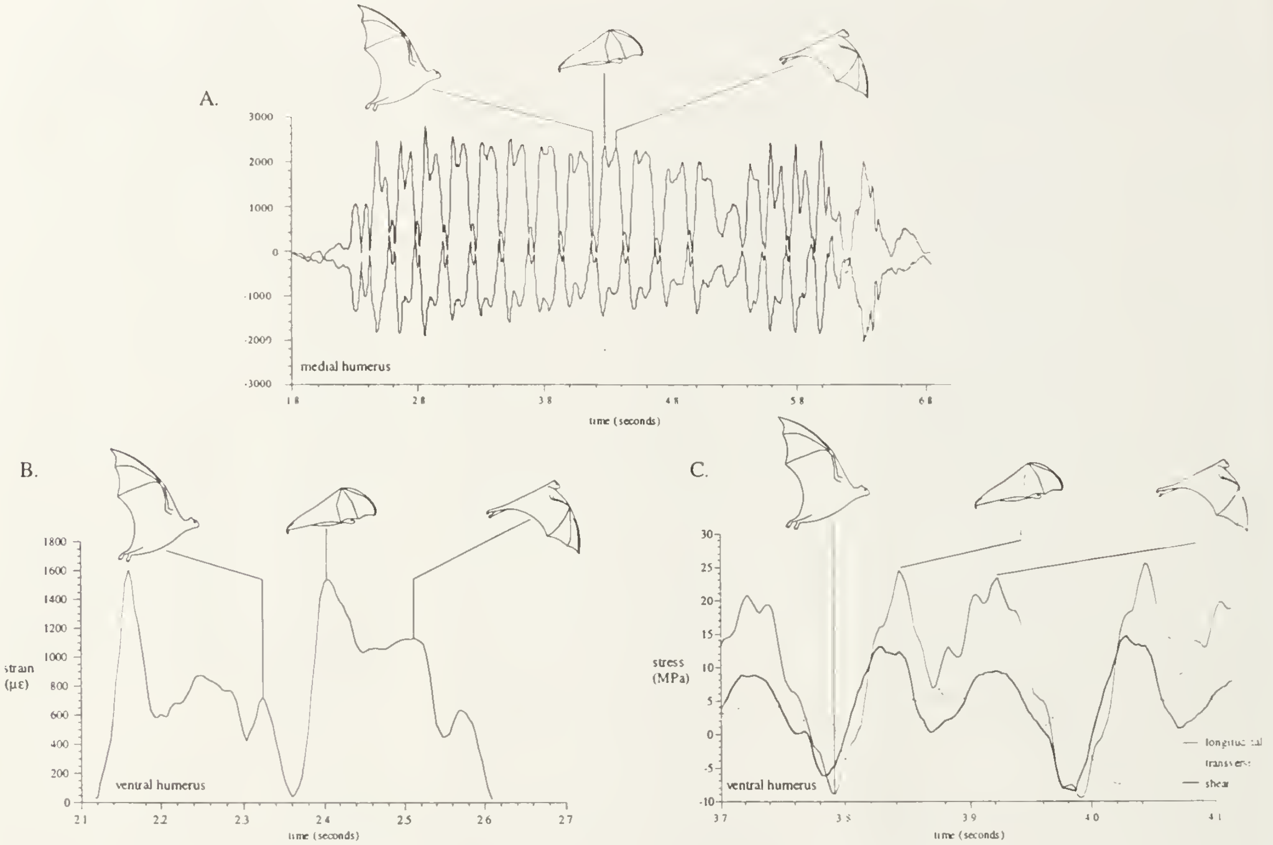


Figure 8. Bat bone strain during flight. A. When we record the surface strains from bone implanted within miniaturized transducers, we see a pattern of regularly increasing and decreasing loading, changing with every wing beat. This illustration shows an entire flight, from take off through level flight to landing. B. The strain from one location on a bat's arm bone is shown here for a single wingbeat cycle. C. From the kind of data shown in B, plus additional information on the properties of bone material, we can calculate the axial stresses along the bone's length (longitudinal) and perpendicular to the bone's length (transverse), and the shear stresses, and look at their changes during flight. In this case, the shear stresses are unusually high for a vertebrate bone, approaching the limits of the bone material.

variety of natural locomotor behaviors. This method, strain gauge analysis, allowed me to surgically attach exquisitely sensitive measuring devices to the bones of my study subjects, and to monitor how bone stresses change during different ways of using the limbs. The results of these analyses have allowed the evaluation, for the first time, of the importance of the unique loading regime associated with suspensory locomotion as a mechanical constraint on the evolution of forelimb skeletal design in primates. I have been able to demonstrate that the loading of the gibbon skeleton is 1) unlike loading regimes predicted from simple theoretical analyses alone, and 2) completely unlike normal skeletal loading of any other mammals. These results, combined with comparative morphological analyses, have allowed me to identify specific features in the design of the hylobatid limb skeleton that can be explained specifically in terms of the habitual mechanical loading associated with brachiating behavior.

These results led me to turn toward two more specialized groups of organisms: bats and marine mammals. These groups experience very distinctive patterns of limb bone stresses in relation to flying and swimming respectively. We are looking closely at the bones of these groups to further test the hypothesis that skeletal composition and limb bone architecture relate directly to the mechanical demands of locomotion. We have begun to explore the possibility that the mineral content and basic properties of the bones of bat wings and marine mammal flippers differ significantly from other mammals. We are also carrying out the first studies to ex-

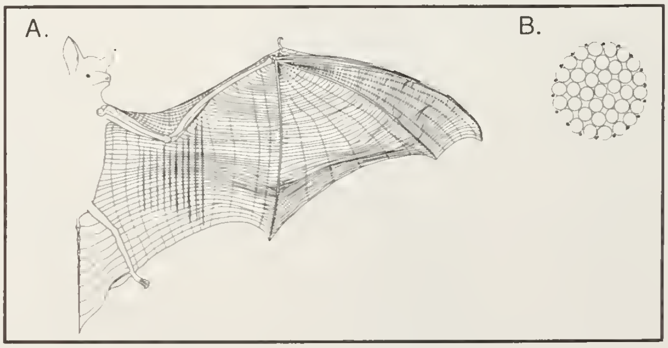


Figure 9. Wing skin architecture. A. The skin of bat wing membranes has remarkable characteristics, unique among mammals. The skin possesses a type of "soft tissue skeleton", a complex network of interconnecting stiff and elastic fibers, that has a characteristic appearance in each species.
B. In cross-section, any one of these fibers has its own complex architecture, comprising an interconnecting set of stiff (collagen) and elastic (elastin) fibers.

perimentally determine the stresses flight places on wing bones.

In particular, our studies of the mechanics of the skeleton in bat flight have produced some surprising results. We have learned that the bones of the wing experience very unusual torsional stresses (Fig. 8). The optimal engineering design to cope with this kind of stresses is to use strucutral support elements shaped as very thin walled cylinders of large outer diameter—the very design we see in some of the bones of bat wings, and in the bones of the wings of birds and pterosaurs, the extinct flying reptiles, as well. Indeed, although conventional wisdom has long proposed that bird wings are "hollow" to reduce their weight, our work on bats suggests that the wing bones of bats and birds alike share these design features because of a need to resist the torsion developed in animal wings.

Several aspects of my research strategy are exemplified by these projects. First, my approach uses comparative morphological studies to address functional questions; it is founded on the development of specific, testable biomechanical hypotheses that permit the development of explanations which go beyond simple structure/function correlations (Fig. 9). My research uses the theoretical background of biomechanics to frame explicit, quantitative predictions about functionally important features of morphological systems. By doing so, it is possible to isolate those features of morphology that are functionally critical, and therefore, of major evolutionary importance and to understand the effects of size in the mechanical analysis of musculoskeletal form.

My work seeks to provide a mechanistic explanation for the adaptation of musculoskeletal form to specific functional requirements. This approach involves the measurement of cross-sectional geometries and curvatures of bones, surface areas of joints, and material properties of bones and soft tissues in species of different size, locomotor capabilities, and phylogenetic affinity to investigate functional correlates of limb form. It also requires the application of sophisticated direct measurement techniques such as the use of telemetered strain gauge analysis of bone deformations, force plate analysis, electromyographic recordings of muscle activity patterns, and high speed cinematography. With these techniques it is possible to determine *in vivo* stresses and the forces exerted on a limb during normal locomotion, and to analyze the correlation of these patterns with the details of limb movement patterns.

Third, this approach requires an explicitly evolutionary or phylogenetic viewpoint. Successful analysis of comparative morphological data demands explicit recognition of the fact that biological structure is shaped both by mechanical constraints on form and function and by the particular evolutionary histories of those species of interest. In accord with this philiosophy, I continue to look for groups of animals that represent "independent evolutionary experiments" that can further help to distinguish phylogenetic from functionally related shape constraints.

My present and future research will focus on areas where biomechanical analysis is likely to prove particularly informative and significant for understanding morpholgical evolution. One example of my ongoing work concerns new analyses of factors dictating variation in the perfomance of the skeleton. Bones comprise a mixture of dense cortical and spongy trabecular tissue; this trabecular tissue consists of a three-dimensional meshwork of interlocking plates and struts that are widely believed to be designed to effectively resist typical bone stresses by their arrangement along the bone's internal force trajectories.

I am beginning an in-depth analysis of the determinants and consequences of trabecular patterning, because I believe this aspect of skeletal design is critical to understanding skeletal adaptation and evolution. Fine-scale architecture of trabecular bone likely reflects a level of detail about the transmission of normal skeletal stresses that cannot be seen in a bone's external conformation. Because trabecular architecture preserves subtle alterations in bone mechanics, evolutionary changes in bone function may be observable in trabecular patterning before they are apparent at a higher level of skeletal organization. I am employing principles of structural design derived from engineering to those morphological features that have the greatest effect on the mechanical behavior of bone. I will use this information to analyze how changing trabecular bone morphology influences the mechanical properties and functional capabilities of bones during growth, and to assess the role of developmental changes in bone structure in dictating the mechanical behavior of whole bones during growth.

This research demonstrates how our investigations as evolutionary morphologists can interface directly with the clinical arena. Trabecular bone is of the utmost importance in the clinical realm. Although it comprises only 20% of total adult skeletal mass, its architecture and functional performance is crucially important to both the clinical and the basic biology of bone. In osteoporosis, for example, bone loss with increasing age compromises the structural integrity of the skeleton, with bones increasingly vulnerable to fracture. Much of the clinically important bone loss is localized to trabecular bone, and a very high proportion of the fractures resulting from osteoporotic bone loss occur in trabecular tissue, particularly in the distal radius, proximal femur, and vertebrae.

An individual's risk of fracture during aging will depend on the basic trabecular framework that was laid down in the bones during early development and on the ability of bony tissue to respond plastically to altered activity. However, high activity levels in mature adults, for example, may increase bone deposition on pre-existing trabeculae but will not lead to the creation of new trabecular supports or new supporting interconnections among existing trabeculae. Clinical programs to address abnormal changes in the skeleton, especially in the vulnerable trabecular regions, require more adequate information about the basic patterns of developmental acquisition of adult bone form, and about the key mechanical effects of altered trabecular morphology. Research in our lab, although ultimately concerned with patterns of evolution, can have a direct impact on our understanding of this clinical problem.

Neural Control of Locomotion

G.E. Goslow, Jr., PhD,
Professor of Medical Science

I am a student of evolutionary adaptation. I freely admit that I always have been and probably always will be. While in graduate school I studied the functional anatomy of various birds of prey. I had the opportunity to make some high speed films of these birds attacking and striking their prey and recently while previewing some of these with my students, I still found myself in awe of a goshawk's ability to alter so quickly, and with such grace, its entire body orientation in space within a single wing beat. This split-second precision requires a complex interplay of the sensory and motor components of the flight apparatus and left me wondering in 1965, as it does today, how such precision is accomplished and how it evolved. At the time I was making these films in Davis, California, and students were protesting on the Berkeley campus, I read a series of papers by Elwood Henneman and his colleagues which provided us with a coherent, testable hypothesis for why muscles may contain more than one functional kind of motor unit. Recall that a motor unit consists of an alpha motoneuron and its associated muscle fibers (the muscle unit). Henneman's size principle hypothesis states that the size of a motoneuron's cell body determines its recruitment threshold, its recruitment threshold determines the use of the motor unit, and the unit's function or 'usage' determines the type of muscle fiber required for the task[19]. That did it. I had a conceptual window through which to formulate questions of muscle adaptation and after further training in the experimental techniques necessary to pursue neuroanatomical and neurophysiological studies in vertebrate animals, I was ready. My approach to the study of such questions is empirical; I observe the locomotor behavior of the animal, study the organization and behavior of whole muscles *in situ* and measure the neuroanatomical and neurophysiological properties of the smallest functional unit of locomotion, the motor unit.

In the spring of 1986, Ken Dial (University of Montana), Farish Jenkins (Harvard University), and I made a series of recordings of a flying pigeon which substantially influenced my research program from then until now. The recordings were electromyograms from two parts of the largest single muscle in a bird's body; the pectoralis. As in humans, the pectoralis arises from the sternum and clavicle (wishbone) and inserts onto the deltopectoral crest of the humerus (Fig. 10). The pectoralis is essentially the only muscle acting to depress the wing during the power stroke and as a result, provides both the lift required to counter gravity and the thrust required to give the bird an airspeed. The particularly striking features of our recordings which captured my interest were two; 1) the level of activity during takeoff and landing was substantially more 'intense' than during level flight, and 2) there existed relatively more 'large spikes' in the electromyographic bursts associated with takeoff and landing than associated with level flight (Fig.11). So what?

At the time we made this record, we knew the fiber composition profile of the pectoralis muscle of pigeons: 10 –12% large, anaerobic fibers of a mean cross-sectional area of 80 μm; 88-90% small, aerobic fibers of a mean cross-sectional area of 40 μm (Fig. 12). The

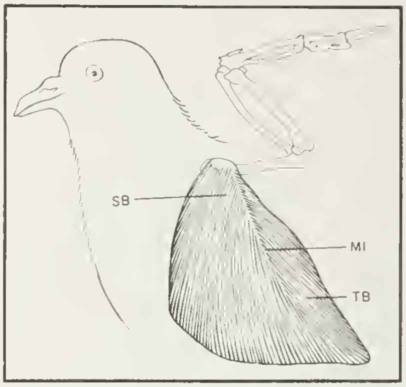


Figure 10. Anatomy of the pectoralis muscle. A: Lateral view of the pectoralis to illustrate its division by a fascial plate, the membrana intermuscularis (MI), into the sternobrachialis (SB) and the thoracobrachialis (TB) heads. The fascicles of the SB arise from the clavicle and anterior sternum, traverse primarily in the dorsoventral direction, and insert on the cranial surface of the deltopectoral crest of the humerus. The fascicles of the TB arise from the posterior and lateroventral surfaces of the sternum, are primarily oriented horizontally, and insert just caudal and more proximal to the tendon of the SB (After Dial et al., 1987)[25].

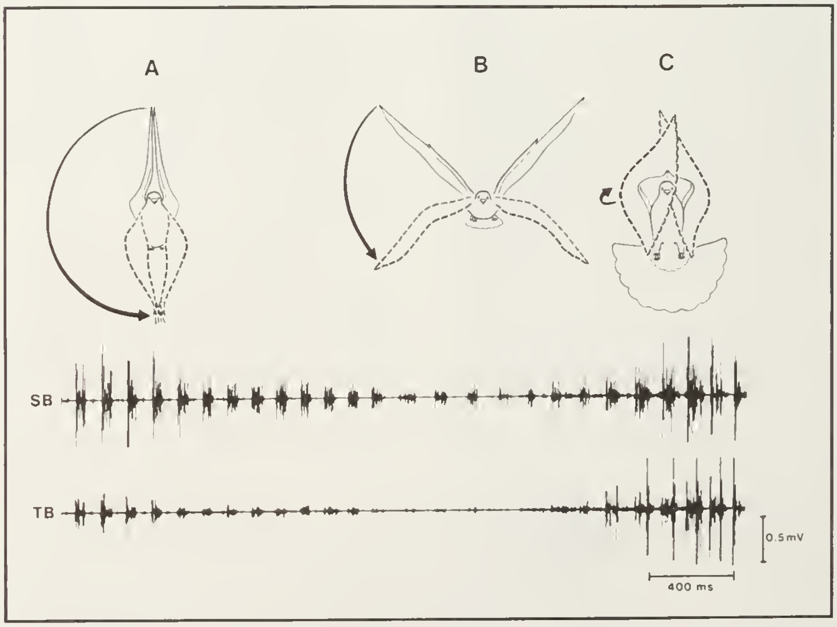


Figure 11. Wingbeat amplitude and body orientation for three modes of flight in anterior perspective: A: Acceleration following release from hand, large wingbeat amplitude, body angle near horizontal. B: Fast flight, small wingbeat amplitude, body angle near horizontal. C: Landing, large wingbeat amplitude, body angle near vertical. The corresponding electrical activity of the sternobrachialis (SB) and thoracobrachialis (TB) portions of the pectoralis is shown below. Large-amplitude spikes in both heads early and late in the sequence are suggestive of the activity of the large, fast glycolytic fibers (After Dial et al., 1987)[25].

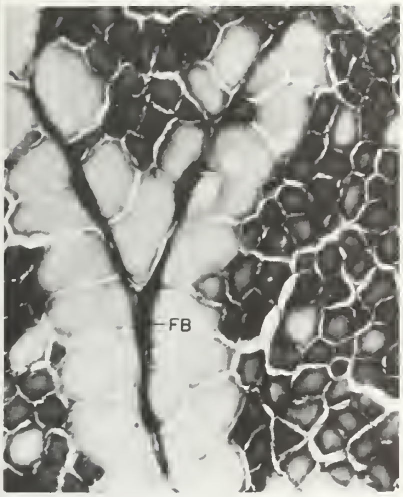


Figure 12. Large and small muscle fibers in the pectoralis of the pigeon. Frozen section (20 µm) from the sternobrachialis head of the pectoralis and stained for myofibrillar ATPase following acid preincubation (pH 4.35). The small, fast oxidative fibers are numerous and tend to be surrounded within the fascicle boundary (FB) by the relatively large, fast glycolytic fibers. Respective mean fiber diameters of 33.5 µm (S.D. ± 8.5) and 78.2 µm (S.D. ± 10.8) for the two fiber types result in a ca. 5.5 x difference in cross-sectional area. Bar = 200µm. (After Dial et al., 198725)[25].

changes in electrical 'intensity' we observed could only reflect variation in motor unit recruitment within this relatively 'simple' power muscle and I began to wonder just how the neuromuscular machinery might be organized to produce this pattern. We also knew that the 'spike amplitude' from two muscle fibers of different size but equidistant from the recording electrode will be relatively larger for the large fiber[20,21]. And as amateur bicyclists somewhat familiar with the principles of gearing, we were aware that for maximum efficiency, there is a close match between a muscle fiber's contraction rate and its biochemical composition[22]. Armed with this information, coupled with our knowledge of fiber morphology and presumed physiology within the pectoralis, we set out to investigate more fully the nuts and bolts of wing design and control.

Dr. Alan Sokoloff and I executed a series of detailed studies of the morphological and physiological properties of the motor units of the pectoralis muscle of pigeons. Our techniques of study involve *in situ* isolation of an individual motoneuron, its stimulation, and the recording of the mechanical properties of its associated muscle unit. Properties such as twitch contraction time, maximum tetanic force and fatigability are measured. When we repetitively stimulate a single motoneuron to the point where its muscle unit will deplete its glycogen stores we can subsequently identify individual fibers by histochemical methods. In this way, we are able to correlate fiber morphology and biochemistry (large and anaerobic vs small and aerobic) with physiological contractile properties (fast or slow, large or small, high endurance or low endurance).

In addition, and perhaps of particular interest to Rhode Island's clinical community, we are able to determine the muscle unit's architecture within the parent muscle. A relatively unappreciated point about the structure of many relatively long, parallel fibered muscles found in all vertebrate groups (including humans) is that individual fibers often do not traverse the entire length of the muscle fascicle. (A recent report of this architecture in human sartorius and gracilis, accompanied with a thorough review of this literature as it pertains to humans may be found in a 1993 report by Heron and Richmond[23]). Our reconstruction of isolated muscle units within the pigeon pectoralis reveals that almost no fibers traverse the entire origin-to-insertion distance, but instead, lie somewhat in-parallel to one another, are of variable length, and are scattered among fibers of other units (Fig. 13). Since individual fibers do not traverse the entire origin-to-insertion length, they must be embedded to some extent in a collagen/elastin framework[24]. This realization over the past few years has added an interesting if not puzzling twist to our theories of motor control.

Dr. Gary Kamen from the Department of Physical Therapy, Boston Uni-

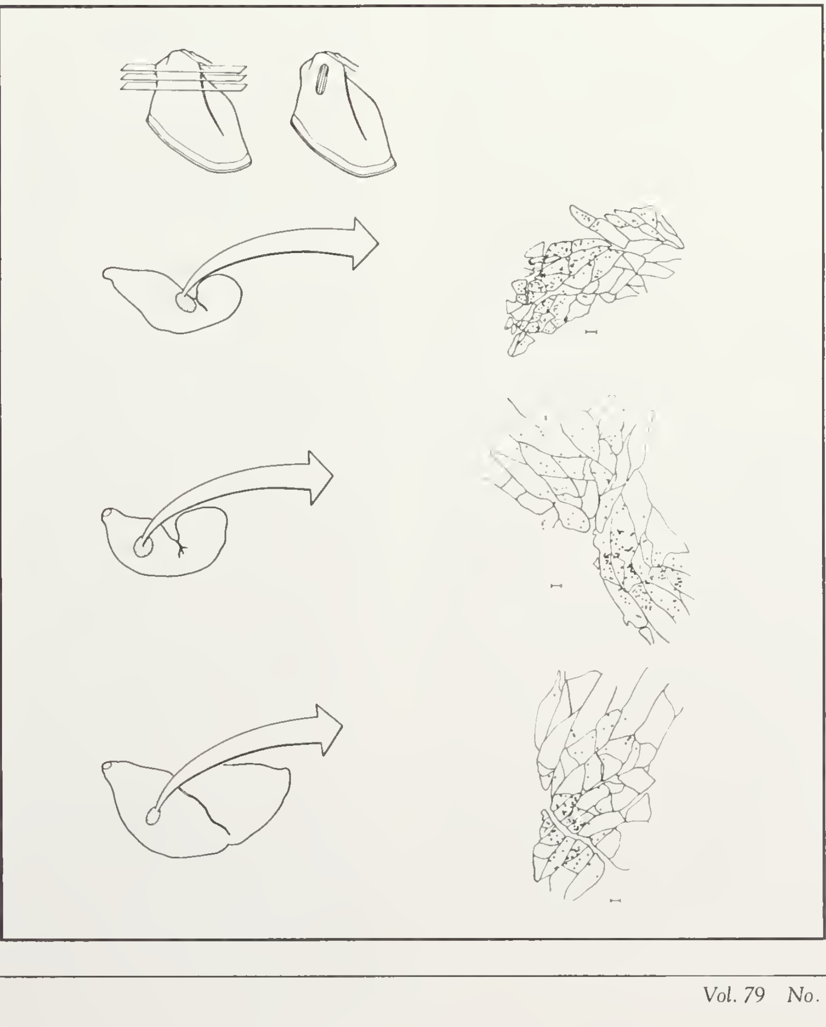


Figure 13. Top two icons represent the pigeon pectoralis in lateral perspective (see Fig. 10). The left depicts the cross-sectional levels at which the muscle unit fibers are viewed and the right the origin-to-insertion extent of the unit (shaded). The three remaining illustrations each show the whole muscle in cross-section (left) and fibers of the unit in association with its adjacent fascicles (right). Note the decrease in number of fibers from proximal to distal.

versity, and I are collaborating on a study to determine the *in vivo* firing frequencies of the two kinds of muscle units present in the pigeon pectoralis. Dr. Kamen routinely records electromyograms from human subjects of various ages, employs techniques for decomposing the complex electromyographic wave form into the spiking patterns of the constituent motor units, and looks at the effects of aging on motor unit size and firing pattern. If successful in our collaboration, we will be able to address some of the questions posed concerning unit recruitment during takeoff, level flight and landing in birds and in addition, perhaps, learn something about motor unit usage during the long migration flights characteristic of many species. I must say, our early experiments have been a challenge.

Other studies are on-going in our laboratory that relate to more global issues of evolutionary adapation. In collaboration with a graduate student in our program, Chris Kovacs, and Dr. Ron Meyers at Weber State College in Ogden, Utah, we are examining the locomotor apparatus of a group of seabirds which use their wings to 'fly' in air as well as under water. Puffins, murres, razorbills and some other lesser-known birds belong to the family Alcidae; they are collectively known as alcids. The alcids are of particular interest from a functional standpoint in that they use their wings for both under water and aerial propulsion. Since the density of water is 1000X that of air, this is a real trick. One naturally asks the question: Has there been an "evolutionary compromise" in these species such that they either fly efficiently in air, but not in water or vice-a-versa? Just recently, we collected some slow motion sequences of several species flying in air and under water for kinematic analysis. We have learned that the wing beat frequency under water is 2-5X slower than that in air which suggests the possibility that there may exist two gears of motor units; one set for water and one set for air. On a recent trip to Iceland, we collected muscle tissue samples from the flight muscles of the Atlantic Puffin for histochemical analysis. We have only begun to process the tissue, but at first glance, there does indeed appear to be two populations of fibers within the pectoralis. If so, the question of whether or not these fibers are differentially recruited remains. If they are differentially recruited, through what mechanism of neural circuitry is this accomplished? How do wing kinematics of the alcids compare to those of typical aerial flyers or to those of the most specialized of the under water flyers, the penguins?

To pursue these questions and other similar ones, we need careful observations of these birds behaving in both mediums. To this end, we will use a variable-speed wind tunnel presently available in our laboratories. In addition, we just received word from the National Science Foundation that our department will receive funds to build a relatively large water flume for studies of marine and fresh water organisms. Funds also have been appropriated to us for a high-speed video system that will enable the recording of rapid events (wing beats) easily and efficiently.

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The Next Five Years

G.E. Goslow, Jr., PhD, Professor of Medical Science

HUMAN MORPHOLOGY AT BROWN

I began teaching biology in 1967, but I am a relative newcomer to medical education; soon I will accept the final examination papers of my fifth gross anatomy class. Teaching medical students has been an interesting and stiff challenge. As I scrambled to prepare for this challenge, I was surprised to discover that medical education in this country is in its infancy when compared to education in the liberal arts[1]. The dawn of the 1800s in America saw only four medical schools to supply the physicians we needed. These schools and subsequent ones granted their degrees after only a few weeks to one year of instruction (exclusively lecture). Any pressure to improve and lengthen the curriculum at a particular school resulted in financial stress; students simply enrolled someplace else. It was not until 1859 that Lind University in Chicago (later Chicago Medical College and presently Northwestern University) raised its entrance requirements and lengthened its academic year to five months. Little support from other schools came until 1871 when Harvard University instituted a three-year curriculum, a nine-month academic year, and written and oral examinations. Their enrollment dropped by more than 40%, but they held out. The major turn came in 1893 when Johns Hopkins University established a four-year curriculum complete with laboratories for instruction and some integration of the university and hospital facilities. This Hopkins model was accepted and spread to other schools around the country. To a person who has been teaching for almost 30 years, 1893 was yesterday. My maternal Grandmother was already a young woman.

Although the American Medical Association had been in operation for over fifty years, it was not until 1904 that it established what was to become its Council on Medical Education. Among other things, the Council convinced the Carnegie Foundation for the Advancement of Teaching to evaluate our system of medical education and report back. The 1910 report, written by Abraham Flexner a student of American higher education, was far from flattering[2]. The Flexner report resulted in an infusion of Carnegie money into the better schools around the country (many inferior ones closed their doors), and more-or-less established the educational pattern followed by most medical schools at the present time. Again, 1910 is not so long ago and it is not surprising that we continue to struggle with how best to educate future physicians.

Two years after beginning studies...the graduate students are fully engaged with their discipline and excited about the future whereas medical students tend to be exhausted and resentful of the basic sciences.

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Our struggles of the past few years have resulted in a revolution within medical school curricula across the country. This is generally known as "medical school reform". Public health policy, the teaching of ethics and 'problem based learning' are the associated clichés you have read and heard about. In a recent review of the situation from a national perspective, Eli Ginzberg[3] provides a thoughtful summary of the reform. He divides it into five major components which call for: 1) Integration of basic sciences into clinical instruction, 2) Look to developmental biology (and genetics?) to serve as the integrator, 3) Recognize the importance of population-based medicine, 4) Make room in the curriculum for considerations of ethical principles at every stage of decision making, and 5) Inform all clinical decision making with an awareness that dollars are scarce and will become scarcer. If you are so inclined, read Ginzberg's paper; it is a scholarly and critical synopsis of the general state of affairs.

There is no question that our group will pay attention to the times and continue to alter and adjust our course to meet the needs of our students. Ginzberg's first two points pertain specifically to anatomy as a basic science and require our focus. But meeting the needs of our students these days is no easier than it was in Flexner's day and the best path is not evident. We all realize the predicament we are in when it comes to teaching information; our knowledge base is escalating so rapidly that it is difficult to know what and how much information to teach. To make matters worse, many of us recognize the need to teach much more than just factual information to our students. What to leave in, what to cut out? More and more students are entering medical school with less and less exposure to the traditional sciences; how does this impact on the path we as educators should follow?

Discussions reach much deeper than curriculum content. In a particularly thoughtful analysis, Chris Leadem from the University of Arizona compares and contrasts our approach to the way we educate graduate students vs medical students[4]. He begins by noting that both groups of students are the best and the brightest when we accept them into our programs. Two years later, however, the graduate students are fully engaged with their discipline and excited about the future whereas medical students tend to be exhausted and resentful of the basic sciences. Perhaps medical students should not be taught at all by experts in any field; where have all the generalist teachers gone[5]? Maybe the traditional lecture and textbook are completely out of date[6,7] and then again, maybe they are not[8].

These issues are not only debated at the national level, but at the grass roots level as well. Just last week the first year students at Brown called a meeting of the basic science faculty to discuss a variety of issues relating to the curriculum for the first two years. They are concerned; we are concerned. Within Brown's administrative structure in the School of Medicine there is considerable energy and thought directed to these issues. The School is embarking on a curriculum reform initiative known as **MD 2000**, a competency-based curriculum which addresses not only content across the curriculum, but student abilities as well such as communication, problem solving, and diagnosis. An enlightening summary of the essence of Brown's curriculum reform written by Smith and Fuller[9] is available from the office of the Associate Dean of Medical Education, Box GA218, Brown University, Providence, RI 02912.

We are cognizant of many of these debates, and we will continue to pay attention to adjust our educational approach in Human Morphology. The truth is, I suspect we will continue to struggle for as long as our culture evolves and our scientific frontiers are pushed back. As the struggle continues, however, our group at Brown will try to remain focused and sensitive to the needs and, whenever possible, to the wishes of our enthusiastic, highly motivated students whose aspirations are simple; to become the best physicians they can be.

INEVITABLE CHANGE

As we begin our sixth year at Brown, several major changes will be evident. Dave Carrier will be leaving to accept a tenure-track position at the University of Utah. Dave will be sorely missed by the medical, undergraduate and graduate students he has touched here. His educational style is not only unique, it is almost magical. Dave's approach to teaching conveys a refreshing curiosity and excitement that captures the student's imagination and serves to motivate them.

Joining our Morphology group this summer will be Steve Gatesy. Steve's initial teaching responsibilities include standing with Sharon Swartz and me as a primary instructor in Human Morphology. Suffice it to say that anybody who spends a summer month traipsing around Greenland searching for vertebrate fossils, runs a top-flight experimental laboratory in functional morphology, and graces his publications and lectures with exquisitely prepared illustrations, has got to be interesting. We look forward to working with him.

The growing pains of curriculum are bound to be felt by us all. Adjustments in the second year course schedule effective in the 1995–96 academic year will prevent these students from coming back to help us in the anatomy laboratory. The void created will be immense and we hope only temporary.

We will continue to reach out to the Brown clinical community to assist in any way we can. Our group has experienced substantial intellectual growth through participation in our hospital-based programs. Financial constraints have us all on the run and may well affect our programs in the next few years. Adjustments to allow our Morphology faculty to teach more undergraduates and interact more closely with graduate students are being made which, of course, impacts on what we are able to do on other fronts. Along with our Deans and Clinical Chairs, we are exploring ways to effectively meet all of these needs and I am confident we will succeed. We have been fortunate in the support we have received in our early years, and we look forward to a prosperous next five years.

ACKNOWLEDGEMENTS

I personally owe a debt of gratitude to several of my colleagues who so graciously gave of their time, energy, advice and confidence. For offering suggestions, sharing materials and ideas and simply giving of their experience, a simple, but heartfelt "thanks" to John Cronan (Brown University), Art English (Emory University), Marty Felder (Brown University), David Greer (Brown University), Farish Jenkins, Jr. (Harvard University), Chris Leadem (University of Arizona), John Cooke (University of Massachusetts), Steve Smith (Brown University) and Phil Ulinski (University of Chicago).

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Public Health Briefings

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Judith Feldman, MD, and John P. Fulton, PhD

The Most Restrictive Alternative

Janet O'Connell, RN, MPH, Program Manager, Tuberculosis Program, Division of Disease Control, Rhode Island Department of Health

The proper management of an individual with tuberculosis (TB) is dependent upon a variety of factors. Aside from an appreciation of host factors, these include identification of suspected disease, appropriate history taking, physical exam, radiologic exam, identification of the organism, determination of antibiotic sensitivity of the organism, prescription of an appropriate chemotherapeutic regimen, and the adherence of the patient to the prescribed regimen. The current standard regimens recommended by the American Thoracic Society and the Centers for Disease Control and Prevention include, at a minimum, a four drug induction therapy regimen followed by a multiple drug maintenance phase. Depending on organism sensitivity, the maintenance phase is recommended for at least 6 months, with a range of 6 to 27 months or more. TB generally cannot be cured unless an appropriate course of treatment is followed.

The frequency of medication administration varies, but most regimens are either daily or twice weekly. Doses are calculated by body weight, to a maximum, and involve more and larger pills than the average patient may be accustomed to taking for an infectious disease. Also, the medication must be taken for much longer periods than others prescribed for infectious disease. For example, a daily regimen for an organism of unknown sensitivity in an 80 kilogram person would be 10 1/2 pills in the induction phase, and if the organism were determined to be fully sensitive, 7 pills in the maintenance phase. Even if the organism were fully sensitive, the maintenance phase would require biweekly doses of 5 pills each. In the event of any first-line drug resistance, none of the aforementioned options apply. Treatment then becomes far more complicated, labor intensive, toxic, and costly. To optimize bactericidal effect and to prevent the selection of drug resistant organisms, all medications in each dose must be taken at one time. Side effects, from inconvenient to incapacitating, are frequently reported.

TB is often aptly referred to as "a social disease with medical consequences." Many other social and medical co-morbid circumstances impinge on the patient concurrently with the diagnosis of TB. Extreme poverty, addictive disorders, homelessness, mental illness, and other medical issues such as AIDS and cancer often hinder adherence to TB treatment.

DIRECTLY OBSERVED THERAPY

Because of the substantial prevalence of drug-resistant TB in the northeastern United States, difficulty with adherence to treatment regimens, and the severity of treatment side effects, the standard for the treatment of TB in Rhode Island is Directly Observed Therapy (DOT), in which a trained health care provider personally delivers each dose of medication to the patient and observes the ingestion of each dose throughout the entire course of therapy. This approach assures treatment to cure, prevents relapse, and eliminates continued transmission of TB in the community. Most persons accept DOT, motivated by a concern for their own well being, and the well being of others with whom they come in contact.

The Rhode Island Department of Health (the Department) and the state subsidized TB Clinic have a collaborative program which helps patients follow prescribed therapeutic regimens. Program staff provide intensive case management and direct service to each person reported with TB throughout the course of therapy.

THE MOST RESTRICTIVE ALTERNATIVE

In a very small minority of patients, community-based care with maximal support is ineffective in assuring adherence to prescribed therapeutic regimens. Infrequently, an individual with documented TB cannot or will not accept treatment as prescribed.

In the event that an individual refuses to comply with DOT, Rhode Island General Law 23-10-6 allows the Director of Health to issue a compliance order, requiring the individual to complete an appropriate prescribed course of medication for TB. In the event that all less restrictive options have failed, or were considered and determined to be not feasible, the Director has the option to issue an order for the removal of the patient for detention in a hospital or other suitable treatment facility, if there is a substantial risk of transmission to others. The Director of Health or her designee is the only person empowered to issue such an order in Rhode Island.

Within 72 business hours of such a detention, the Department must provide "clear and convincing evidence" that detention is necessary. The individual subject to detention is entitled to be represented by legal counsel. The procedures clearly outlined in the statute provide for due process and protect the civil liberties of the individual. A detention order must be renewed every 45 days by the Director throughout the course of detention, with appropriate

ABBREVIATIONS USED

DOT	Directly Observed Therapy
TB	Tuberculosis

evidence that the detention continues to be necessary.

INVOLUNTARY TREATMENT PROHIBITED

The statute does not permit forcible administration of medication. No person, for any reason, may be compelled by the Department to undergo treatment for TB, as long as the individual is willing to place him/herself in an environment that excludes others from the risk of acquiring TB.

REGIONAL RESOURCES

The detention and sequestration of persons with TB was an accepted consequence of the diagnosis as recently as the early 1960's. With the advent of effective antibiotics and community-based care in the mid-1960's, however, such drastic and disruptive measures came to be considered unnecessary. As a result, the infrastructure to provide such care was dismantled in Rhode Island. TB treatment centers do exist in the Northeast (the Lemmuel Shattuck Hospital's TB Treatment Unit in Boston and the Goldwater Hospital in New York City are examples), but reciprocal agreements must be executed to allow detention orders to be effectuated across state lines. Enabling legislation, to be submitted in the 1996 session of the Rhode Island General Assembly, will facilitate this process, when enacted.

LESSONS LEARNED

During the most recent resurgence of TB and the emergence of drug resistant TB, hard lessons have been learned. Cure cannot be expected if appropriate treatment recommendations are not followed. Inadequate treatment can lead to disastrous consequences, as fatal outbreaks of multi-drug-resistant TB have demonstrated.

TB is a largely preventable and curable disease. However, it does not permit multiple failed attempts at treatment. Such failures have spawned incurable forms of the disease, including strain W TB, resistant to seven or more drugs. Recognition of this danger has led to a paradigm shift in the treatment of TB, including DOT with maximal support, detention if adherence to prescribed treatment is not assured, and control options that cross state lines to achieve economies of scale.

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Health by Numbers

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Jay S. Buechner, PhD, and William J. Waters, Jr., PhD

Trends and Patterns in Health Insurance Coverage, 1991-1994

The reimbursement system for health care in the United States has been examined at the highest policy levels in recent years, from the perspectives of system reform, expansion of coverage, and containment of costs, especially costs in the public sector. The perceived problem is that the health care system represents nearly 14 percent of the nation's economy and per capita expenditures on health are 50 percent higher than in any other country, while over 15 percent of the population remains uninsured for health care costs. (National Center for Health Statistics, 1995; Bureau of the Census, 1995).

In Rhode Island, the level of insurance coverage has consistently been higher than the national figure, but there is evidence that the number of uninsured has increased in recent years. Telephone surveys of Rhode Island adults (ages 18 and older) show the percentage of uninsured increasing from 8.5 percent in 1991 to 11.3 percent in 1994 (Figure 1), a change that is statistically significant with a level of certainty greater than 95 percent. (Office of Health Statistics, 1995a).

The likelihood of being insured for health care costs is strongly dependent on income, with lower income persons in Rhode Island being more likely to be uninsured than higher income persons (Figure 2). At the lowest income levels, the effect of income is moderated by the availability of coverage through public programs such as Medicaid. The highest percentages of uninsured adults fall among the "working poor," with incomes between $10,000 and $19,999. Nearly one in four persons in this income range have no coverage, compared to approximately one in forty among Rhode Islanders making $35,000 or more.

High percentages of adults with no health insurance are seen in minority sub-populations in the state, among whom general health status is often compromised compared to the rest of the state's population (Office of Health Statistics, 1993; Office of Health Statistics, 1995b). In 1994, persons in minority groups were two to four times more likely to be uninsured than were white, non-Hispanic adults in Rhode Island (Figure 3). Among Hispanic respondents, the percentage of uninsured more than doubled between 1992 (17.1 percent) and 1994, while the percentages for other minority groups did not change significantly. During the same

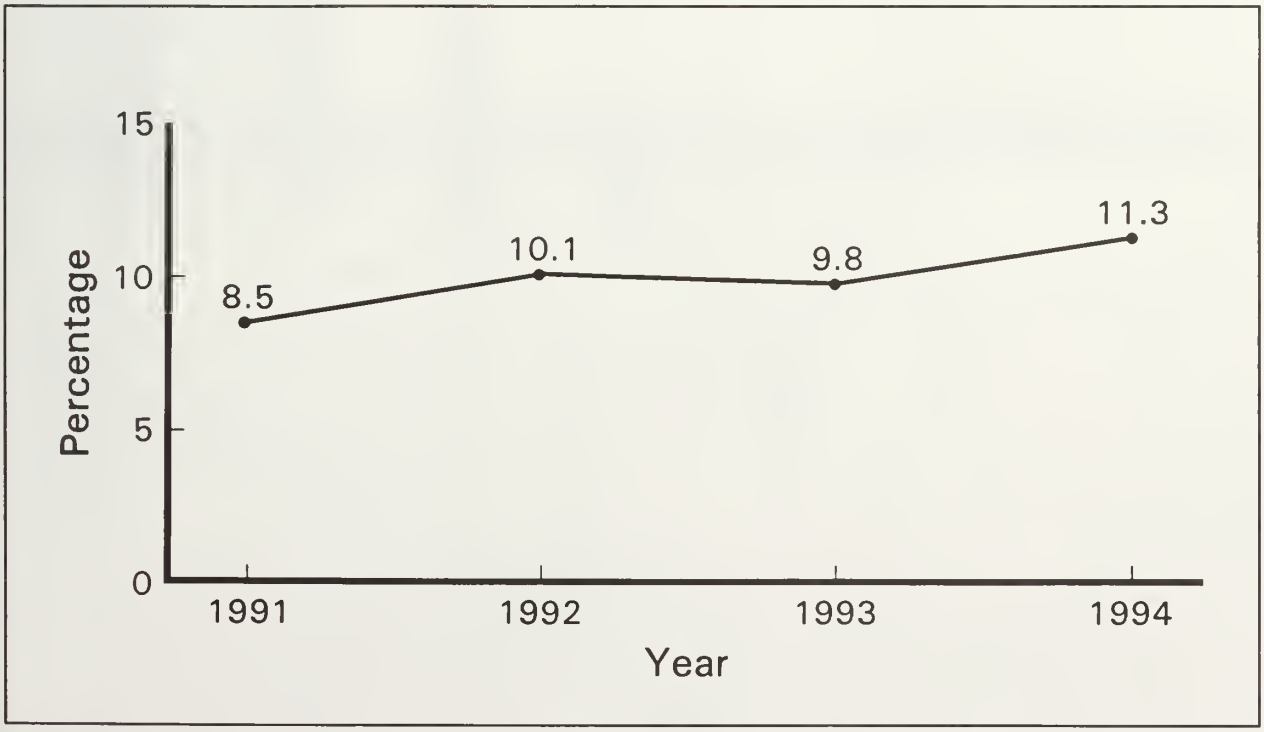

Figure 1. Percentage of Persons Ages 18 and Older without Health Insurance Coverage, Rhode Island, 1991-1994.

time period, the proportion of Hispanic respondents in the survey increased from 2.6 percent to 6.1 percent, suggesting that the lack of health insurance may be especially high among recent immigrants in this group.

Data from the national Current Population Survey show that 15.2 percent of Americans of all ages were without health insurance through the entire calendar year of 1994. (Bureau of the Census, 1995). The survey placed Rhode Island sixteenth among the 50 states and District of Columbia with 11.5 percent uninsured. The difference between the figures for the state and the nation is statistically significant. During the period 1991-1993, however, the Current Population Survey reported the proportion of uninsured in Rhode Island as 10.0 percent, ranking tenth among states and supporting the pattern of increasing numbers of uninsured found in data collected at the state level.

An increasing number of uninsured persons often results in problems for both public health and for the health care system. Lack of insurance coverage strongly affects access to primary and preventive medical care, including routine prenatal and pediatric care, with potential adverse health consequences. In addition, the state's health care system treats acute and emergency conditions among this population without reimbursement, and the costs of this care are shifted to other patients or revenue sources, which are limited in their capacity to support such care.

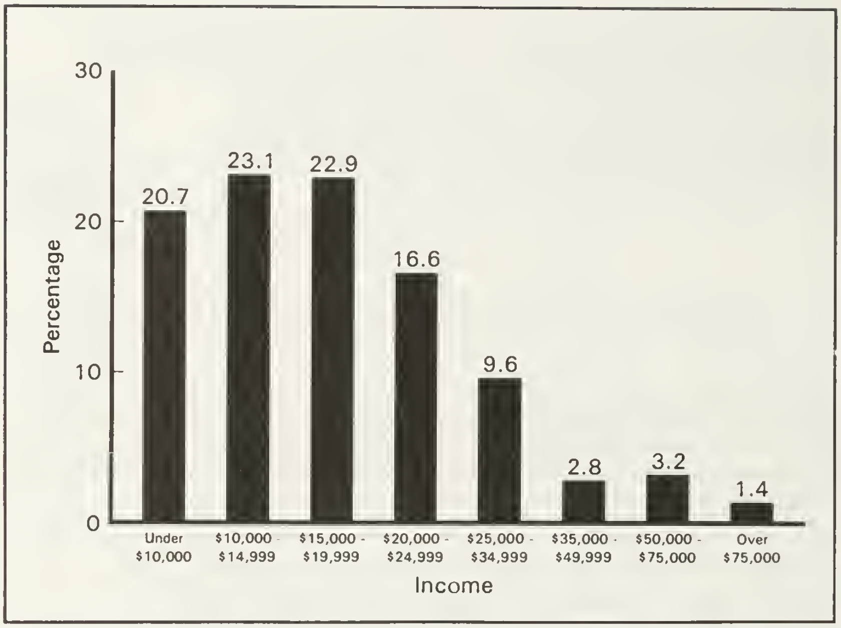

Figure 2. Percentage of Persons Ages 18 and Older without Health Insurance Coverage, by Family Income, Rhode Island, 1994

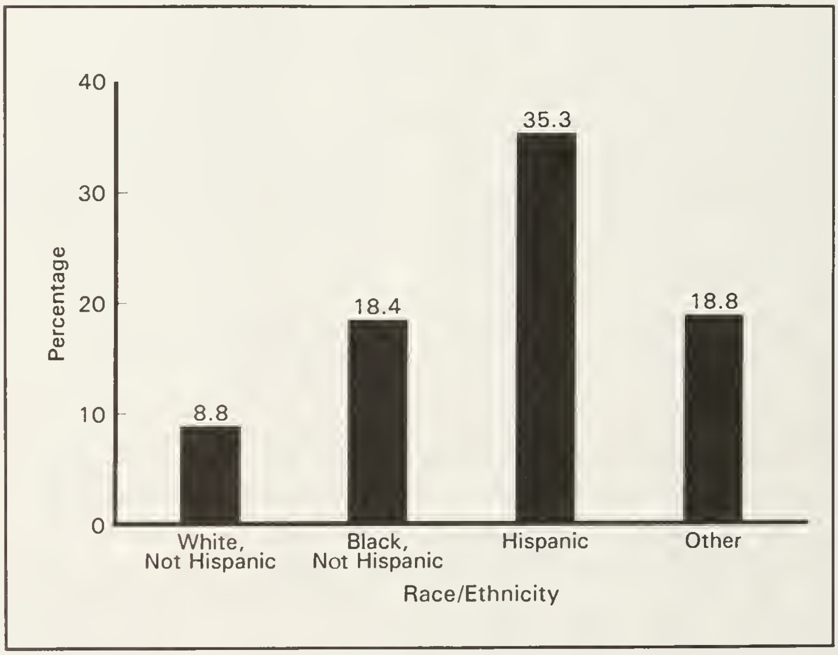

Figure 3. Percentage of Persons Ages 18 and Older without Health Insurance Coverage, by Race/Ethnicity, Rhode Island, 1994

SOURCES

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Vital Statistics

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Roberta A. Chevoya, State Registrar

Rhode Island Monthly Vital Statistics Report
Provisional Occurrence Data from the Division of Vital Records

Vital Events

	Reporting Period		
	July 1995	12 months Ending with July 1995	
	Number	Number	Rates
Live Births	1,304	13,936	14.0*
Deaths	806	9,640	9.7*
Infant deaths	(8)	(86)	6.2#
Neonatal deaths	(8)	(68)	4.9#
Marriages	836	7,003	7.0*
Divorces	304	3,506	3.5*
Induced Terminations	444	5,751	412.7#
Spontaneous Fetal Deaths	95	1,002	71.9#
Under 20 weeks gestation	(90)	(931)	66.8#
20 + weeks gestation	(5)	(71)	5.1#

* Rates per 1,000 estimated population
# Rates per 1,000 live births

Underlying Cause of Death

	Reporting Period			
	January 1995	12 Months Ending with January 1995		
	Number	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	325	3,235	324.7	4,502.0
Malignant Neoplasms	188	2,400	240.9	7,251.5
Cerebrovascular Diseases	57	598	60.0	754.5
Injuries (Accident/Suicide/Homicide)	25	342	34.3	6993.0
COPD	43	389	39.0	240.0

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.
(b) Rates per 100,000 current estimated population of 996,325.
(c) Years of Potential Life Lost (YPLL).

Note: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

THE RHODE ISLAND MEDICAL JOURNAL

The Official Organ of the Rhode Island Medical Society
Issued Monthly under the direction of the Publication Committee

VOLUME 1
NUMBER 1

PROVIDENCE, R.I., JANUARY, 1917

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NINETY YEARS AGO

JANUARY, 1906

The lead editorial expresses grave concerns about ethical standards when physicians testify for contingency fees. The editorial declares: "In the strenuous life which most physicians live, endeavoring to gain a livelihood, the temptation to profit by the multitude of suits brought against corporations and individuals for damages in accident cases is very strong. Too strong in some cases to be resisted, the doctor agrees to testify for a contingent fee and from that moment his testimony is necessarily biased and of little value. It may be ethical, it may be right for a lawyer to suppress unfavorable testimony, to magnify favorable factors, to bully the opposing witnesses and put the desired words into the mouth of his own, to avail himself of all the tricks of his trade to win his case, but it is not ethical and it is not right for the doctor as witness to allow possible pecuniary profit to influence his testimony."

A second editorial reports upon the visible progress made by the Rhode Island Hospital in providing medical care for the greater Providence community. In 1885 the hospital treated 752 patients; by 1905, that number had increased to 4,500 with a daily average of 247 patients. The average stay had decreased from 39 days [1875] to 20 days [1905]. The total expenses for the year 1905 amounted to $155,863.63 while total receipts from all sources amounted to $150,622.93, thus with a yearly deficit of $5,240.70.

This issue lists the deaths of 12 practicing physicians in the Rhode Island community. The average age at death was 53.3 years. Two had been born in Canada but the remaining ten were native New Englanders, five born in Rhode Island.

The lead scientific article, written by Robert F. Noyes, MD, discusses diet in Bright's disease. The author states: "The diet must be such as will nourish the body, preserve the highest type of health and reduce to a minimum the labor of the kidneys." He emphasizes that the planned diet should avoid those foods "deleterious in contracted kidney, particularly alcohol." "It is thought that pepper, ginger, mustard and horseradish have a baneful influence upon the kidney while salt, vinegar and lemon juice do not." "Tea and coffee should be partaken of sparingly as they increase cardiac energy and increase the reading of the sphygmomanometer."

H.G. Partridge, MD speculates upon the relationship of arteriosclerosis to renal disease. While not providing references, the author nonetheless quotes numerous authorities (eg, Gull, Sutton, Osler) showing a close association between the two entities. He then cites a specific case of a 54 year old male with evidence of diffuse arteriosclerosis preceding a fatal interstitial nephritis.

FIFTY YEARS AGO

JANUARY, 1946

George W. Waterman, MD, Chief of Gynecology at Rhode Island Hospital, discusses some practical aspects of recognizing and treating sterility in the female. After a summary discussion of female physiology, endocrinology and histology, Waterman surveys various tests for endocrine activity and concludes: "The Rubin test for patency of the tubes has been discussed as to its diagnostic and therapeutic value as has the lipiodol hysterosalpingogram. Results on total number of cases 248 seen and on 197 cases adequately examined and treated have been given. Particular attention is drawn to the excellent results obtained where the thyroid factor was apparently at fault."

Uterotubography in sterility is discussed by Lawrence A. Martineau, MD. After demonstrating various radiographic patterns of diagnostic merit, the author concludes that radiologic uterotubography is superior to insufflation.

The Presidential Address (Providence Medical Association) of B. Earle Clarke, MD is presented. "Science alone, for a medical man, is not enough," he states. "The spiritual values are still of first importance. Sincerity, sympathy, sobriety, responsibility, integrity, ethics, high moral and social standards are always an important part of the physician's equipment."

The Journal lists the names of 52 local physicians who had recently been honorably discharged from active military duty.

This issue also carries notice of the deaths of 11 local physicians. Average age at death was 59.7 years. Six were born in Rhode Island and another two were born elsewhere in New England.

TWENTY FIVE YEARS AGO

❦ JANUARY, 1971 ❦

This issue is devoted, almost in its entirety, to the modern nurse. A. Rose Frantantuono, RN discusses the practical components of current nursing practice and describes three month courses preparing a woman for simple home-based nursing.

Catherine McGoldrick, RN, outlines the Rhode Island Junior College associate degree nursing program. Of the approximately 450 nursing programs currently admitting students, it is anticipated that many will eventually be based in junior colleges. Barbara Tate, Ed.D., Dean of the College of Nursing at the University of Rhode Island offers the history and purposes of a baccalaureate education in nursing. The University possesses the first such program in the state which is now 25 years in existence. Recently, Salve Regina College and Rhode Island College have also established degree-granting programs in nursing. Catherine Graziano, RN, President of the Rhode Island State Nurses' Association, describes the professional organization for nurses within the state and the efforts made to establish true professionalization amongst practicing nurses. Finally, this issue of the Journal reprints William Osler's essay on the nurse and the patient.

The tarnished image of higher education in the United States and the lack of moral direction currently observed in the collegiate student population is explored by Rev. Joseph L. Lennon.

The lead editorial discusses the current shortage of nurses and identifies various causes for this.

The January issue of the Journal pays tribute to those community physicians who had died during the preceding 12 months. Fourteen physicians are listed, the average age being 71.8 years. The majority were native to Rhode Island. Most received their MD degrees from New England schools but a few attended medical schools in New York City, Philadelphia and Washington, DC.

❦

New Managing Editor

The Publications Committee and Editorial Board of Medicine and Health/ Rhode Island are pleased to announce the appointment, as of January 1996, of Ms. Darlene Trew Crist as our new Managing Editor. Ms. Crist, who has attended both the American University and Providence College, is well known in the Rhode Island community as a writer, public affairs advisor and editor of health care publications. Her office is: 54 Church Lane, Wickford, RI 02852-5004

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Manuscripts will be accepted for consideration with the understanding that they are original contributions, have never been published in its current form, and are submitted only to *Medicine and Health / Rhode Island.* An article should address a substantive issue of interest to the Rhode Island Medical community. Articles may be no longer than 3,000 words in length and have no more than 20 references.

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Providence, RI 02912

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Wickford, RI 02852-5004.

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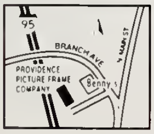

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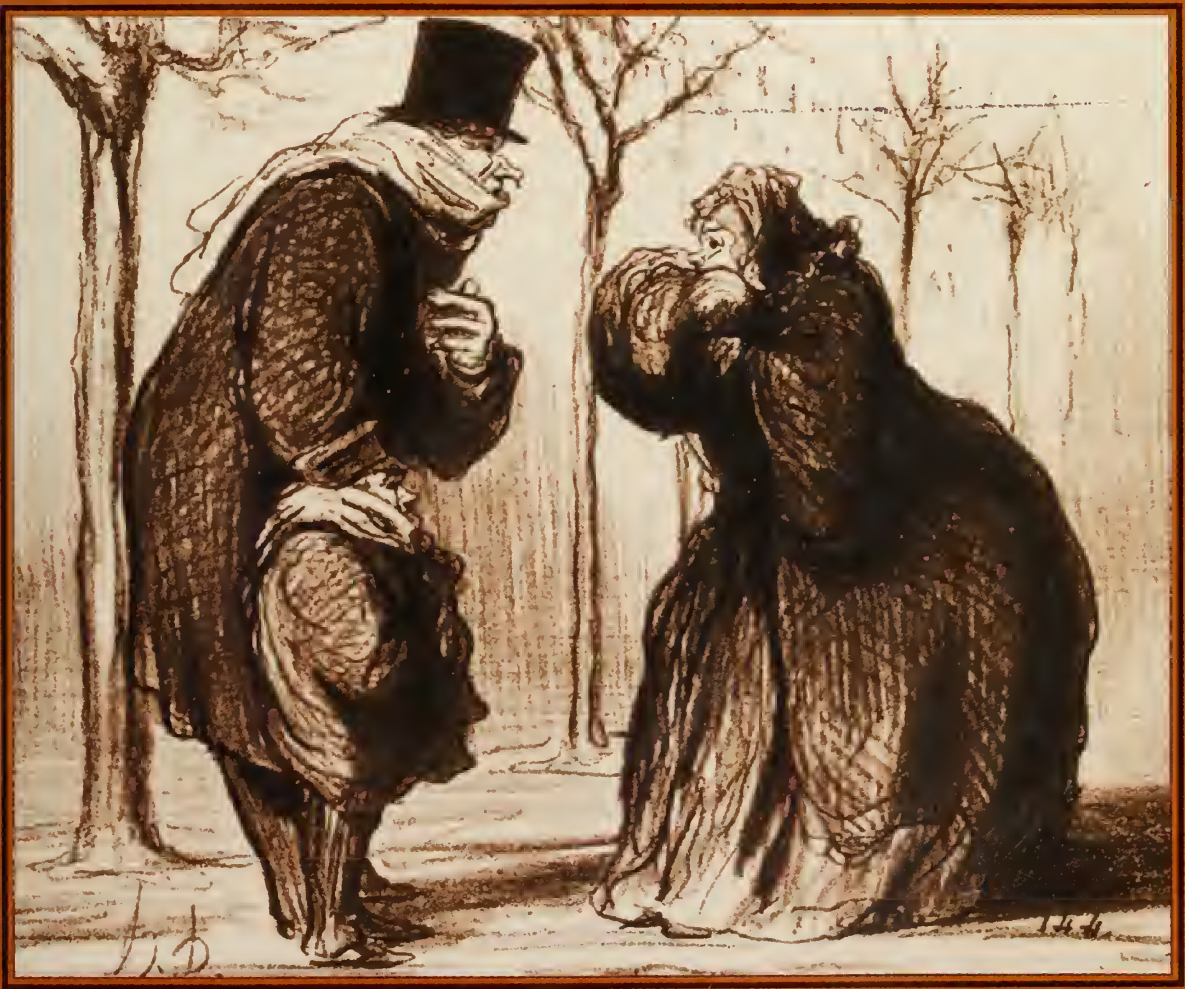

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Cover: An Honore Daumier lithograph dated February, 1858, entitled "Paris Grippe." Translation: "How are you coughing?" "I am coughing quite well, thank you. And you?"

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COMMENTARIES

John Tierney and Medical Philately

For many years John Tierney had been Deputy Director of the Rhode Island Department of Health, an exemplary public servant and a tireless advocate for effective public health measures. In his retirement years, John adopted a new, but not totally unrelated, interest in life. He has become a nationally known authority on stamp collecting as it pertains to issues of disease, disease prevention, public health and those commemorative stamps which illustrate the great leaders of medicine. John has been persuaded to provide this journal with a periodic column discussing philately and medicine. "Medical philately," in John's words, "is much more than collecting bits of paper. It adds many new dimensions to a collector's life and enables him to escape, if only temporarily, from the stressful and unrelenting pressures of the working day. It provides an immediate passage into a therapeutic world of harmony, learning and beauty. This experience increases one's knowledge and understanding of the history of medicine, especially about those gifted ones whose dedicated genius has led to the lengthening of our life span."

This month's issue contains Tierney's first column on tuberculosis and philately.

Bid My Eyes Keep Holiday

The Scriptures most often portray blindness as an unwanted and burdensome event befalling the elderly. Aged Isaac in his sightlessness is deceived by Jacob; and Jacob, too, is incapable of seeing his grandchildren Manasseh and Ephraim when he bestows his patriarchal benediction upon them. Blindness, in these contexts, is viewed as a doleful, irreversible infirmity deserving compassion. Deuteronomy says: "Cursed be he that maketh the blind to wander out of the way." Samson, sightless in Gaza and one of the few Biblical persons afflicted while still in early manhood, is granted one final redemptive act, but generally little was expected of the blind except to suffer in silence.

Few who were blinded had ever talked of what it was like to struggle in darkness. Homer, said to be blind, described noble battles and odysseys of sighted heroes, but offered no insights into sightlessness. On the other hand, John Milton, having lived 43 years before abject blindness overtook him spoke openly, eloquently and often of the burdens of sightlessness.

> *"O dark, dark, dark amid the blaze*
> *of noon,*
> *Irrevocable dark, total eclipse,*
> *Without all hope of day!"*

Instead of retreating to a quiet inner realm, Milton confronted his blindness and recruited whatever latent resources still lingered within him. Indeed, Milton's greatest literary contributions (**Paradise Lost, Paradise Regained, Samson Agonistes**) were dictated while he was totally blind, socially isolated and politically vulnerable. ("God blinded him with his hand, that, like the nightingale, he might sing darkling.") Many writers have since speculated on the origins of Milton's blindness, including Milton himself. And a generation of academic ophthalmologists has reviewed Milton's journals and correspondence to dissect out hints about the precipitating factors in his loss of vision.

John Milton, son of a scholarly musician, was born in 1608, growing to manhood in a tranquil home where learning in the classics was encouraged. He was blessed with a superb education at Cambridge and never in his 66 years of life ever wanted for the necessities of life. In 1638 Milton travelled to Europe. While in Florence he visited blind and infirm Galileo then under house confinement by the Office of Inquisition. References to this encounter are readily found in Milton's copious writings but a visually intact Milton made no mention, then at least, of Galileo's blindness.

Back in England, Milton allied himself with the Puritan-dominated Parliament with whom he shared both religious and republican convictions. When Cromwell assumed authority as Protector during the Commonwealth interregnum, Milton undertook an increasingly important and sensitive role in governmental affairs, drafting many vital trade treaties in behalf of an England increasingly concerned with mercantile affairs.

The first subjective hint of his difficulties in vision appear in Milton's journals during the year 1642. A decade later he writes to a friend: "It is about ten years, I think, since I perceived my sight to grow weak and dim, finding at the same time my intestines afflicted with flatulence and oppression. Even in the morning if I begin as usual to read, my eyes immediately suffered pain and seemed to shrink from reading, but after some moderate bodily exercise were refreshed."

At first Milton ascribed this to mere eye strain brought on by excessive reading and he confided his minimal disability to a small number of confidants, particularly a German merchant transplanted to London, Henry Oldenburg (later to be a guiding force in the activities of the Royal Society and editor of its great periodical, *The Philosophical Transactions.*) When blindness succeeded in impeding his daily activities he made no secret of his advancing infirmity. Milton, indeed, talked openly, obliquely, directly, and certainly metaphorically of what he regarded as his assigned fate. Plentiful allusions to light and darkness; clarity and clouding; incandescence and shadows enrich his political tracts as well as his monumental poetry. Milton forthrightly reconciled himself to his sightlessness, quickly replacing his initial sense of being a chosen victim to one who, with serenity, accepts God's will. "... shall I not cheerfully bid my eyes keep holiday, since such appears to be His pleasure?"

Others in addressing the cause of Milton's blindness, were less charitably disposed. Some contemporaries said that it was clearly the effects of syphilis while others perceived it as divine retribution for an atheistic regicide. In an angry letter to Roger Williams (a great admirer of Milton) a Mrs. Sadleir acerbically declared: "... you should have taken notice of God's judgment upon him, who stroke him with blindness."

Some 60 years ago William Wilmer, MD, ophthalmologist to John Hopkins Hospital, "accepted" John Milton as a patient, summarizing the known information concerning his eye disease[1]:

Personal history: High spirited, sensitive disposition. Headaches in youth. Used his eyes moderately. Suffered from gout spring and fall. Under great strain at time of beginning of eye trouble, his wife having left him in 1643. Blindness began at that time, or a little before, when he was about 34 years old. At 44 entirely blind. Cause of death "gout stuck in" according to account.

Symptoms: (1) Subjective: Headaches in youth. Slowly failing vision beginning in left eye. Great discomfort in using eyes. Colors around light. Smoky appearance in front of eyes. Subjective sensations of light (phosphenes) upon closing eyes while in bed. Micropsia (objects appear reduced in size) left eye. Loss of vision in the left side of left eye. (2) Objective: Externally, eyes normal. Vision blind. Visual fields contracted.

Impression: Blindness from glaucoma simplex (chronic simple glaucoma) for the following reasons: Externally eyes normal, which excludes all acute inflammatory conditions. Pain, none except when eyes were strained. Progress, slow (10 years), bilateral, excludes detached retina and all lesions that occur suddenly. Colored rings around lights, which is a common symptom of chronic glaucoma. Phosphenes not characteristic of glaucoma alone, but they occur in many eye diseases, and even in normal eyes if the lids are closely pressed against the eye with head low in a dark room. Micropsia not characteristic of glaucoma. Possible contributing cause of disease (1) Temperament, (2) Gout, (3) Excessive use of eyes, (4) Nervous strain connected with wife's leaving, etc. (5) Age compatible with glaucoma.

The great majority of Wilmer's colleagues agreed with his presumption of chronic glaucoma, but a few believed otherwise. One eminent ophthalmologist, also confronting Milton across a span of 280 years, declaring with confidence that he suffered from a "spontaneous detachment of the retina, first one eye then subsequently also of the fellow eye as well as congenital myopia of a high or excessive degree, with liquefaction of the vitreous humor and other pathological changes which were the probable predisposing causes." No contemporary ophthalmologist, however, gave credence to the two most prominent conjectures offered during the 17th century: syphilis or divine punishment.

Milton's writings make it clear that his courage and spirit prevailed over self-pity. Following total blindness his work schedule actually increased and he even foreswore his customary afternoon naps, thus abiding by his own poetic words, "Awake, arise or be forever fall'n." When Milton talked of his unseeing state, he observed: "Mine . . . only deprives me of the hue and surface of things, and leaves to my intellectual view whatever they contain of substance and value." But of his relentless enemies, of which there were many, he declared that they, however, are "spiritually blind."

Having survived the Stuart Restoration and its inquisition, the great plague of London, the death of two wives and the recalcitrance of three daughters, his many political enemies, and even the great fire of London, death finally gathered him in 1674. He died, "passion spent and calm of spirits," in a "fit of gout, but with so little pain or emotion that the tide of his expiring was not perceived by those in the room." Helen Keller, not unfamiliar with darkness, said: "Sightless Milton dreamed visions no one else could see. Radiant with an inner light, he sent forth rays by which mankind beholds the realms of Paradise."

Stanley M. Aronson, MD

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Lucina Sine Concubitu

Most humans, by age 12, grudgingly concede that they will probably not live forever. Those somewhat older finally admit that eternal life is accorded only to mythic creatures and certain strains of cancer cells. Yet hope lingers and people will evade reality by seeking backdoors to immortality. Humans with pretensions of talent, for example, secretly pray that at least their accomplishments will outlive them. Most others are resigned to the brevity of life, looking only to their progeny or students as their passport to an everlasting future. Knowing that some part of them continues in another person becomes a sustaining thought; and teaching, siring or giving birth to a child, then, serves as a validating, immortalizing, act in the lives of many.

Theories of how parenthood really operates–the mechanics of reproduction–were more fanciful than real before the 17th century. Concepts of reproductive physiology were generated often by whatever rhetoric best conformed to current cultural belief. If, for example, a social system of male dominance prevailed, then the principal contribution to fecundity was inevitably assigned to the male.

Leeuwenhoek, about three centuries ago, used his primitive microscope to explore a variety of biological fluids. When examining semen he observed the spermatozoan body enclosing refractile structures which he interpreted to be a small embryo, the complete precursor of the future baby. The male sperm was thus seen as the bearer of a congruent homunculus while the egg–the contribution of the female–was viewed as the source of undifferentiated nutrition for the developing sperm. The soul, spirit and structural endowments of the newborn were therefore obtained unilaterally from the father while the mother became the nurturing vessel, the benevolent protectress of the baby's essence. Leeuwenhoek's morphologic observations, it turned out, were far more accurate than his embryologic speculations; but certainly this conjecture of his reinforced the 17th century belief that the dominant creative role was exerted by the male.

Older naturalists speculated, occasionally, that reproduction mights also be accomplished by alternate pathways, that *lucina sine incubitu* (ie, childbirth without coitus) might sometimes prevail. It was a Saxony surgeon, J. Albrecht, in 1701 who claimed to have observed this natural phenomenon in a moth. Owens, in 1849, was the first to use the word parthenogenesis (virginal birth) to denote a procreation without the immediate influence of the male. (The word comes from the Greek, *parthenos*, meaning virgin. Athene, patron of the arts, sister of Apollo, Olympian goddess of wisdom and inventor of the flute, the plow and even the science of numbers was also renowned for yet another attribute: In her lifetime she had effectively repulsed all the predatory advances of various male gods thus remaining eternally undefiled. Athene's preserved maidenhood became symbolic of the invincibility of Athens, the city established in her honor. Her temple on the Acropolis - the Parthenon - also derives its name from the same Greek root, *parthenos*. It is a sad commentary that the famous Athenaeum Club of London, named in honor of a legendary woman, does not admit women to membership.)

Numerous 19th century biologists, avidly observing the biological activities of insects, verified that certain species of moths, honey bees and other insects occasionally reproduced without male participation. The gall fly (*Cynips divisa)*, for example, regularly produced offspring with no male intervention; indeed, all gall-flies of this genus are female. The genus *Aphida* (plant lice) have similarly dispensed with the need for copulation. Geneticists estimate that about 0.1% of all species, particularly invertebrates, employ some form of parthenogenesis in their reproductive activity.

J. Loeb at the turn of this century translated these isolated observations to the experimental laboratory and was finally able to stimulate various unfertilized marine eggs to begin (and occasionally complete) the process of development by certain artificial interventions including the use of hypertonic solutions, temperature variation, the puncturing of the egg membrane or by the presence of such provoking agents as colchicine. His seminal studies demonstrated that the spermatozoon has two separable and independent biological functions: First, to initiate the process of development; and second, to convey male genetic material to the evolving zygote. His experimental interventions could therefore substitute only for the initiating role of the spermatozoon. When this occurs under natural circumstances (ie, the spermatozoon enters the egg but contributes no genetic material), it is then called gynogenesis or pseudogamy.

In some parthenogenic systems, only female offspring are produced (a process called thelytoky, from the Greek *thely-* meaning nipple, but more broadly, meaning female; and *-tokos*, meaning to bring forth into the world); in certain other systems, only male offspring are generated (then called arrhenotoky, from the Greek *arrheno-* meaning male, as in the androgenic ovarian tumor, arrhenoblastoma); and in some, both male and female offspring are generated (then called amphitoky, from the Greek *amphi-* meaning both.) With honey bees, the virgin queen bee will generate only males (arrhenotocia) which are haploid, but when fertilized, will produce only females (drones) which are diploid.

Pincus, in the 1930s, extended the domain of parthenogenesis to include higher vertebrates and even mammals. The older concept of the male as dominant - even essential - participant in the wondrous process of reproduction was now utterly shattered. If a tadpole could be produced by merely immersing an egg in a hypertonic solution of potassium chloride, claims of divinely determined male dominance, even of parity, became understandably shaky.

Thoughts of a future world where parthenogenesis universally prevailed may bring comfort to a small minority of females (those declaring that all coitus represents unwanted intrusion). But to the geneticist it brings only nightmares since parthenogenesis, devoid of any opportunity for genetic diversity except through rare mutation, must be regarded as a dead-end form of reproduction. They view with horror any species, constricted by parthenogenesis, as essentially incapable of change through subsequent generations and hence incapable of evolutionary adaptation. Furthermore haploid creatures are additionally burdened with dangerous, often lethal, recessive genes no longer neutralized by a normal allele.

Two irreconcilably extremist positions emerge: One claiming that only male genetic material passes on to the next generation; and the opposing view holding that in the business of reproduction the male is essentially extraneous. And there are sufficient examples of natural parthenogenesis in the zoological world to give some credence to the feminist bumper sticker: "Woman Needs Man Like a Herring Needs a Bicycle." The realities for higher mammals, however, seem to lie somewhere between those two extremes. But while most species content themselves with a reliance upon one generative mechanism, there is the inescapable fact that ebullient nature devises diverse, and truly wondrous, pathways to procreation.

Lucina sine concubitu may function in plant lice; but in the unsentimental Darwinian world of mammals, especially those species needing all the adaptive genes they can get in order to prosper, only a system with bilateral genetic contributions, yielding innovative new combinations, will work successfully. Despite the fervent belief of adolescents, the sex drive was not created solely for their after school amusement; when it comes to competitive survival, sex is very serious business.

Stanley M. Aronson, MD

IRV, sGaw, Raw, and Other Matters

Those of my friends who are real historians and can read medieval Latin texts excite in me the mortal sin of envy. With a dictionary in hand and some recall of four years of high school Latin, I believe I could make it if only the monkish scribes in those dark and drafty scriptoria had not used so many abbreviations and such odd symbols. For example, St. John's Gospel in the Gutenberg 42-line Bible, certainly a copy of a manuscript, begins:

In principio erat verbü:
& verbü erat apud deû:
et deꝯerat verbü.
Om̃nia p ĩpm facta sunt:
& sine ipo factum est nichil.

Not bad, but, but believe me, it gets worse; the inflected endings fade off into nothing, and all sorts of peculiar little symbols. Couple that with Gothic letters that hardly match Jensen's Venetian type for clarity, and comprehension is remarkably impaired.

Something like this obscurity generally developed to set apart the powerful, learned, and priestly classes of society. The ancient Egyptians had two forms of writing: hieroglyphics, which means temple writing, and a cursive demotic form for ordinary people. In the early centuries of the present era, Greek was the language of the upper classes in the Western Empire, and Latin was the vulgar tongue. Yet Latin became the language of scholarship in Western Europe until the early years of the last century. William Harvey used it in his lectures, except when the ancient tongue couldn't stand the strain, then he reverted to English, as in his 1616 Lumleian lecture where he asserts "as by two clacks of a water bellows to raise water" in his Latin text, describing the passage of blood through the lungs and heart to the aorta.

In my medical school days, we still used those beautiful symbols for ounces, drams, scruples, and grains, and lower case Roman numerals for amounts — all centuries old. And we proudly learned the meaning of esoteric combinations of letters such as t.i.d., q.i.d, a.c., p.c., and h.s. Sometimes there was a barbaric mix of Latin and English as in "Seconal gr iss at hs prn DNW." The delicious thing was that only the initiated knew what all that meant. There was even an HHH enema (high, hot, and hell of a lot) for desperate situations.

Medical editors receive manuscripts replete with this kind of thing, but now in 1990s style. There is a list of abbreviations in the AMA Manual of Style, accompanied by the admonition to always spell out at first use. The list is obsolete one year after it has been published. Dictionaries of medical abbreviations are published; yet not more than 60 percent of acronyms that appear in submitted manuscripts ever make it to these dictionaries. I recall laboratory tests of 50 years ago: CF&TT, VDB, II, WSS, and GA&BD. Unexpanded, these intruders would render papers from time to time that are incomprehensible today.

In "Letters to the Editor" in this journal, a gastroenterologist complains of the exuberant growth of acronyms and other jargon, and has included a copy of a letter written by a nurse practitioner that shows how far this plague has spread. I think I betray no confidences by reproducing five lines of her letter:

> The patient was sent from the echo lab to the cath lab. Coronary angiography revealed (LM-10% distal, LAD-proximal 80%, Cx-70% before OM1, RCA-proximal 70%, normal LV). Surgical intervention was recommended. CABG was done on (date) (CABGx6, Ao-PDA-LVbr, Ao-OM1-OM@.Oa-Diag, LIMA-LAD). . .

As I read this, I cannot shake the impression that the writer did not have a human being in mind at all, only a procedure, and even that not in three-dimensional clarity, but rather as a piece of a procedure with neither a past or future. Apart from being incomprehensible to most physicians other than cardiac surgeons, it seems to me that language of this sort (if indeed it is language) diminishes the writer's view of the world and is, in fact, dehumanizing. This letter, as part of a medical record, has no staying power; 10 years from now it might as well have been written in runic characters.

No doubt Standard English does not work for mathematics, nor for prescribing elementary particles like quarks and mesons. Immunologists may pull off such clusters as CD10 (nT,nB;gp100)J5 because they have to; no other way to do it. Try spelling that out for first use! But for most clinical reports, Standard English is the best thing going and its use forces the writer and reader both to comprehend and communicate. Besides obscuring, arcane language says clearly, "Hey, we're smarter than you guys." Worse than that, its habitual use dehumanizes in a profession that ought to be the most humane of the sciences.

Robert U. Massey, MD

(from *Connecticut Medicine*, October 1995)

The Conscience of Thomas J. Hodgkin

In 1926 an American pathologist extracted tissue samples from six museum display jars located in the Gordon Pathological Museum of Guy's Hospital, London. These six autopsy-derived blocks of preserved organs (undisturbed in their glass containers for 94 years) had been originally displayed by Dr. Thomas Hodgkin and had formed the morphological basis for his 1832 description of the disease which now bears his name. Through the use of modern microscopy augmented by special staining procedures, and abiding by histologic criteria proposed by Sternberg and Reed 35 years after Hodgkin's death, the 1926 analysis concluded that only three of the six specimens were indeed Hodgkin's disease. Of the others, one was tuberculosis, one syphilis and one a non-Hodgkin's lymphoma.

Skeptics smugly viewed this veiled putdown as evidence that Hodgkin's accomplishment was flawed and that the eponym bearing his name represented yet another example of misplaced courtesy. In an era where searching for feet of clay has become a major avocation of the intelligentsia, it seems entirely proper, then, to examine this English physician's activities and judge whether his contributions do indeed deserve the enduring recognition that has been accorded to him.

Thomas Hodgkin was born in a village just north of London on August 17, 1798, the first living son of Quaker parents. His father was a private tutor and a skilled mathematician; his mother was learned in Latin and many Western languages. Thomas was raised in a nurturing, deeply religious atmosphere, part of a family which regarded learning as a moral responsibility. The core principles of the Society of Friends - personal discipline, order and simplicity - were the esteemed agenda of the Hodgkin clan.

As a youth Thomas showed an aptitude for languages and the natural sciences. By the age of ten he had determined to become a chemist, with Humphrey Davy as his role model; and by age 18 he was fully apprenticed in a thriving pharmaceutical business.

Hodgkin's youthful interests, however, were broader than the pursuit of a profession. By 1818 he was expressing deepening concerns for the welfare of oppressed native populations particularly those Africans pressed into slavery and transported to the Western Hemisphere. The survival of native American populations, then called the Native Indians, represented yet another of his moral convictions. This intense involvement in the abolitionist movement and the cultural integrity of "aboriginal tribal peoples" became Hodgkin's life-long pursuit. In an essay written when he was but 20, Hodgkin declared that the North American Indians "faced extermination as a consequence of the 'civilizing' influence brought by the settlers and traders from Europe." Years later he was one of the English leaders in promoting a reverse migration of enslaved Africans, particularly back to the independent nation of Liberia; and by 1863, in an England which generally favored the South, Hodgkin was a highly vocal advocate of Lincoln's Emancipation Proclamation, even suggesting that the Commonwealth of Virginia be ceded to the four million emancipated black freedmen.

A career in chemistry, Hodgkin believed, might be too isolating a vocation and in 1819 he enrolled in the medical school of Guy's and St. Thomas' Hospitals. Three years before, Richard Bright, chronicler of renal disease, and John Keats, sometime poet, had also attended this distinguished medical school. The educational sequence, however, proved to be inadequately rigorous and in 1820 Hodgkin transferred to the more demanding medical school of the University of Edinburgh. Here too he experienced the curriculum to be unchallenging and particularly lacking in supervised bedside instruction. In 1821 he travelled to Paris to continue his studies at La Charite and Necker Hospitals, studying as clinical clerk under the tutelage of Rene Laennec. In the summer of 1823, Hodgkin returned to Edinburgh to present his graduation thesis on the physiology of enteric absorption (some 78 pages of dense Latin text) and then to receive his doctoral degree. In 1825, after six years of study in London, Edinburgh and Paris, Hodgkin finally entered the private practice of medicine in East London serving also as a volunteer physician at the London Dispensary, a large facility providing essentially free medical services for the urban poor.

In 1828, when Guy's Hospital medical school seceded from St. Thomas' Hospital, Hodgkin was appointed as its first lecturer in morbid anatomy and museum curator, a teaching post he held with increasing distinction for ten years. It was during this highly productive decade that he contributed so materially to the belief, novel at that time, that compelling correlations existed between clinical presentments and underlying pathological changes. His two volume text on the morbid anatomy of serous and mucous membranes was published in 1836; his inaugural description of acute appendicitis with perforation and peritonitis as a clinical entity, in 1829; his celebrated monograph on disorders of the aortic valve, also in 1829; his published studies (with J.J. Lister, a Quaker wine merchant and father of Joseph Lister) on the use of the achromatic microscope, in 1830; his published arguments that Asiatic cholera was a contagious disorder (contrary to prevailing judgment), in 1831; and in 1832 his memorable paper on "some morbid appearances of the adsorbent glands and spleen" wherein he offered details of a fatal, non-tuberculous disorder with non-caseating enlargement of lymph nodes and spleen. About 30 years later Wilks designated this entity as Hodgkin's disease.

During this interval of intense academic activity, Hodgkin's interest in the welfare and education of North American Indians continued unabated. He authored a succession of widely read, trenchant pamphlets on issues of social justice, chaired numerous action committees and personally underwrote the schooling of many Cree Indians. In addition, he became involved in the design and supervision of the newly established University of London, a place of higher education, unique at that time, that did not require its students to adhere to a designated religious faith. In a manner remarkably similar to the social priorities of Rudolph Virchow, his contemporary in Berlin, and Benjamin Rush of Philadelphia, also an alumnus of Edinburgh, Hodgkin involved himself in contentious issues of public health, child nutrition and the merit of universal free education especially of impoverished populations. He invested much of his energies in dispensary medicine and evening classes for the laity. His fervent writings on issues of public sanitation and personal hygiene included pamphlets against smoking and alcohol while favoring exercise, both physical and intellectual. His non-medical writings were imbued with a socially responsible, religious fervor much like the lay tracts of Rush or Parkinson.

In 1837, Dr. Thomas Addison was promoted to the post of Physician to Guy's Hospital thus opening a vacancy as Assistant Physician. Hodgkin applied for the position but was ultimately rejected in what his peers believed to be an egregious, politically motivated decision. Hodgkin promptly resigned from the hospital and medical school, devoting the remainder of his career, almost three decades, to his more deeply rooted commitments in behalf of the abolitionist movement, public health advocacy, the welfare of indigenous peoples (particularly the Native Americans of northern Canada) and his burgeoning general practice.

Toward the end of his life Hodgkin, a devout Quaker, developed a close friendship with Sir Moses Montefiore, a prominent London philanthropist and patriarchal advocate of Jewish affairs. The two travelled the world extensively, Hodgkin acting as the personal physician to the Montefiore family. Long before Herzl promoted the philosophy of Zionism, Montefiore had encouraged and supported the return of landless Jews to Palestine, then an underpopulated, infertile, malarial backwater province of the Turkish Empire. Montefiore also financed housing projects in Jerusalem [many still in existence] as well as self-sustaining communal farms in the Galilee. In addition, he established a charity hospital and a school for girls in Jerusalem, using funds from the Touro legacy. Hodgkin's narrative of his visits to north Africa and the Middle East, supplemented by his exquisite watercolor landscapes of the Mediterranean region, was published a few years after his death.

In the spring of 1866, prompted by news of a renewed outbreak of cholera in the Holy Land, Hodgkin and Montefiore resolved to visit the region again. They disembarked in Alexandria and began the arduous overland trek to Jerusalem. Hodgkin took ill in the coastal village of Jaffa, his sickness probably an exacerbation of his chronic, recurrent enteritis. Within days, however, it was accompanied by tenesmus, fever and delirium possibly representing a superimposed cholera infection. He died quietly on April 4, 1866. Montefiore outlived his beloved friend by 19 years; and on his 100th birthday in 1884 was honored by the Jewish community of New York City by the establishment of a chronic disease hospital in his name. Eighteen years before, Montefiore had an obelisk erected to keep the cherished memory of his close companion. The monument, situated in the outskirts of Tel Aviv, bears, in part, this inscription:

HERE RESTS THE BODY OF THOMAS
HODGKIN, MD, OF BEDFORD SQUARE,
LONDON. A MAN DISTINGUISHED
ALIKE FOR SCIENTIFIC ATTAINMENTS,
MEDICAL SKILLS AND SELF-SACRIFICING
PHILANTHROPY. HE DIED AT JAFFA THE
4TH OF APRIL, 1866, IN THE 68TH YEAR OF
HIS AGE, IN THE FAITH AND HOPE
OF THE GOSPEL.
HUMANI NIHIL A SE ALIENUM PUTABAT.

Stanley M. Aronson, MD

Laboratory Study of Breast Cancer Using Conventional and Molecular Cytogenetics

Hon Fong Louie Mark, Ph.D., F.A.C.M.G. and Kirby I. Bland, M.D., F.A.C.S.

Breast cancer is the most common form of cancer in women in the United States. According to the National Institutes of Health (NIH), the average mortality rate for breast cancer in the U.S. is 27.5 per 100,000. Approximately 46,000 women in the U.S. were expected to die of breast cancer in 1993[1]. The incidence of breast cancer is steadily rising although its true cause is unknown. According to the National Breast Cancer Coalition, 1 in 8 women will get breast cancer in her lifetime, up from 1 in 14 in 1960. If the trend continues, at least 1 in 7 women will be affected by the year 2000.

Few dispute that breast cancer is an urgent national health problem. According to the National Breast Cancer Coalition: "This year, a new case of breast cancer will be diagnosed every three minutes, and a woman will die from breast cancer every 12 minutes." The Coalition also reports that more women have died of breast cancer since 1960 than twice the number of all Americans killed in World Wars I and II, the Korean, Vietnam and Persian Gulf Wars combined. Forty-eight percent of these deaths occurred within the last ten years. Since breast cancer increases with age, its incidence is expected to rise as the "baby boom" generation enters middle age. The loss of human and financial resources due to breast cancer — already of staggering proportions —will most certainly escalate if left unimpeded.

In spite of the significant effect of this disease on the health of half of the people in our nation, the number of cases of breast cancer studied cytogenetically in the U.S. and elsewhere is disappointingly inadequate[2]. This is mostly related to the advanced level of expertise required to culture and analyze limited quantities of tumor material, in general, and breast cancer tissues, specifically. Some of the technical difficulties encountered include, but are not limited to, difficulties in establishing culture, contamination, overgrowth of abnormal tumor tissue by normal stromal cells, low mitotic index (insufficient metaphases), suboptimal GTG-banding and complex aneuploidy. Of available cytogenetic information, most has been gathered from highly advanced tumors, often metastatic lesions or effusion material[3]. Only partial karyotypes are available in half of the cases. In the majority of human breast cancers with full karyotypes, a large number of unidentifiable markers were reported. Furthermore, the cytogenetic analysis of breast cancer cases suffers from the serious drawback of artificiality of the *in vitro* culture systems[4]. The study of breast cancer either in a controlled human *in vitro* system or by utilizing recently developed, newer techniques will therefore complement other forms of analysis.

As many are aware, cytogenetics is the only procedure where the results of genetic damage can be directly observed using bright field and fluorescent microscopy. Recent developments in molecular cytogenetic technology offer an unprecedented opportunity for the study of breast cancer on relatively more abundant archival material. We will describe two areas of laboratory investigation of breast cancer using conventional and molecular cytogenetic techniques that are promising.

CYTOGENETIC STUDY OF GENETIC INSTABILITY IN BREAST CANCER CELLS UNDER NORMAL OR ADVERSE ENVIRONMENTAL CONDITIONS

A fundamental question in cancer research has been: What characteristics differentiate a normal cell from one that is malignant? The difference between a normal cell and one that would eventually become cancerous may or may not be detected under normal circumstances. When adverse environmental conditions are present, the difference in the behavior of a normal and a malignant cell may become more pronounced. The interaction of the genetic background and factors in the environment in the genesis of breast cancer is a virtually unexplored area of research.

> *Recent developments in molecular cytogenetic technology offer an unprecedented opportunity for the study of breast cancer on relatively more abundant archival material.*

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For the past two years, researchers at Rhode Island Hospital's Laboratory of Cytogenetics have been conducting genotoxicity research using certain tree condensates in collaboration with the Maine Toxicology Institute. Wood-drying condensates are by-products of the kiln drying of trees, which is a major activity of the timber industry in the U.S. with virtually unknown environmental consequences. Genotoxicity research in the area of wood-drying conducted in this laboratory represents the only human testing information currently available in the U.S. and elsewhere, as the Maine Toxicology Institute leads the nation in the effort for characterizing these wood-drying compounds. We plan to use this unique stystem and baseline data derived in the past two years to study the interaction

ABBREVIATIONS USED

CA:	Chromosome aberrations
DNA:	Deoxyribose nucleic acid
FISH:	Fluorescent in situ hybridization
GTG-banding:	G-banding using trypsin as the proteolytic enzyme treatment and Giemsa as the stain
NIH:	National Institutes of Health
SCE:	Sister chromatid exchanges

(HER-2/neu, Ki-ras, p53 and c-myc are specific names of genes, not used as abbrev.)

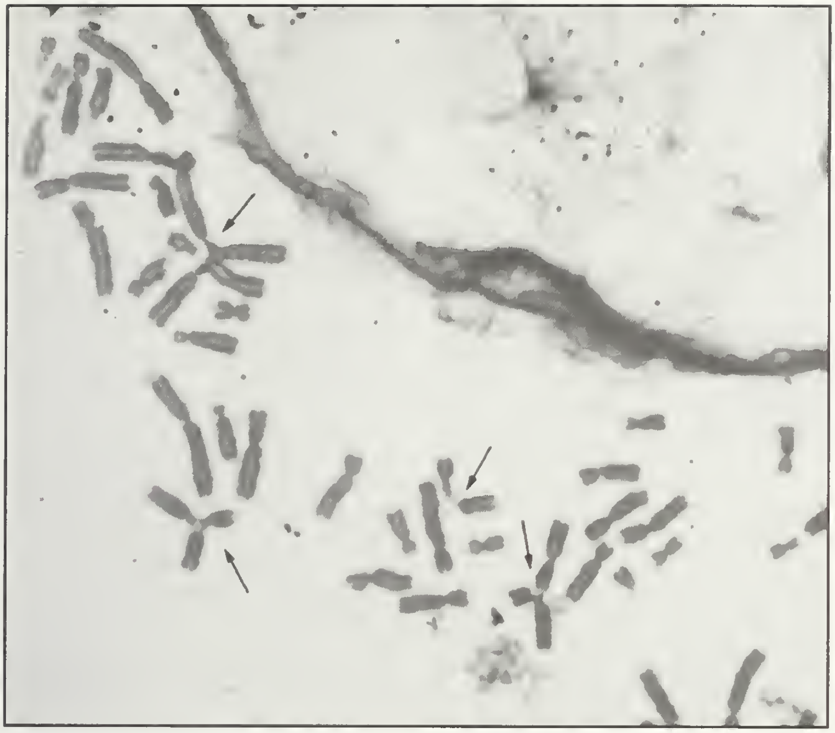


Figure 1. A human metaphase illustrating chromosome aberrations.

of the genetic background and environmental genotoxicants in breast cancer cells.

Genetic instability, whether constitutional or acquired (for example, induced by environmental genotoxicants) has long been suspected as a factor that predisposes a cell to cancer. Genetic instability in the form of chromosome aberrations (CA) (Figure 1) and sister chromatid exchanges (SCE) (Figure 2) has been studied by a number of investigators[5,6, 7]. Various authors have reported high SCE incidence in patients with various types of neoplasias[8-19]. In addition, studies have confirmed the sensitivity of SCE in response to physical, chemical and biological stimuli[20-22]. An unequivocal association between either CA or SCE and breast cancer, however, has not yet been established.

Livingston et al.[12] found that women with active breast cancer have a significantly higher mean SCE frequency in their somatic cells than control women or women with greater than five years of post-treatment for breast cancer. They studied 125 patients and the mean SCE rate was based on a count of 30 cells. Previously, Husum et al[23] studied SCE in peripheral lymphocytes in women with and without cancer of the breast and detected no difference, although a statistically significant, positive correlation between SCE and cigarette smoking was found.

Adhvaryu et al[24] studied spontaneous and mitomycin-C-induced rates of sister chromatid exchanges in 40 patients with cancer of the breast and 40 controls. They reported that the SCE rate per cell in lymphocytes of patients with breast cancer was higher than in the controls and was significantly reduced after surgical removal of the tumors.

Husain[25] studied 22 patients with breast cancer as well as 10 normal, healthy, age-matched controls. An apparent increase in the average rate of SCE per cell was observed with the advancing stage of breast cancer. Although promising, this topic has only begun to be explored.

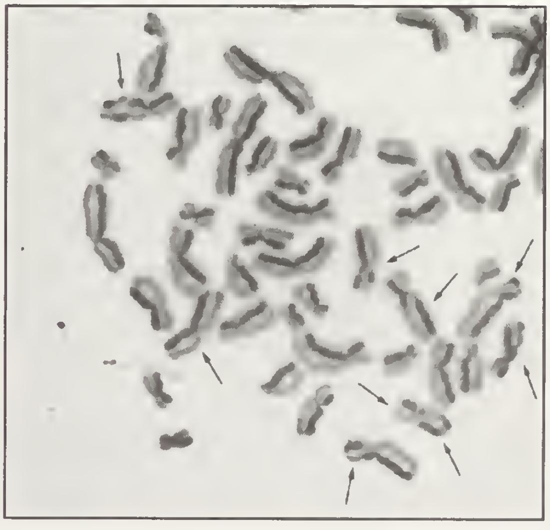
Recently, in Italy, Bonassi et al[26] investigated whether chromosome aberrations in circulating lymphocytes were predictive of future cancer onset in humans. These investigators found statistically significant increases in the standardized mortality ratio for all cancers in subjects with medium and high levels of CA in peripheral blood lymphocytes, and urged the prevention (or at least a reduction) of environmental exposures that can cause an increase in chromosome aberrations. Long-term effects, however, are still uncertain. Preliminary findings by Sorsa et al[27] in a prospective follow-up study suggested that subjects with a high percentage of structural chromosomal aberrations may be at an elevated risk for cancer.

Dhillon et al[28], using 20 breast cancer patients and 50 controls and a one-way analysis of variance, found the mean values of SCE per metaphase to be 5.8, 4.69 and 5.98, respectively, in breast cancer patients before surgery, one month after surgery and after a three-year follow-up. These findings are significant.

There is a need for additional information on the association of an elevated level of genetic instability and breast cancer and the interaction of breast cancer cells with genotoxicants present in the environment. One of our research goals is to study the above in a defined *in vitro* system. An abnormal response of cells from breast cancer patients to environmental genotoxicants can yield valuable insight into the molecular mechanisms of carcinogenesis and genetic and environmental interactions involved in the genesis and the multi-step progression of breast cancer. It will create challenges and opportunities for effective strategies for breast cancer prevention.

Cytogenetic assays are being used to accomplish our study goal. Use of these assays to detect chromosome instability is not new. They have been used extensively to survey the exposure of humans to genotoxic agents. The conceptual basis has been the assumption that the extent of genetic damage re-

Figure 2. A human metaphase illustrating sister chromatid exchanges.



flects critical events for carcinogenesis, such as an impaired ability to remove damaged DNA. An increased level of chromosome aberrations has been found to be a relevant biomarker for future cancer risk (see, for example,[29]). Cytogenetic assays to measure chromosome damage have been evaluated and validated in this laboratory[30] and applied for genotoxicity testing[31,32].

Our aim is to establish whether genetic instability, in the form of chromosome aberrations, aneuploidies or increased levels of SCE, can serve as potential biomarkers for breast cancer. The need for reliable prognostic indicators is especially urgent in axillary node-negative breast cancer. Adjuvant systemic therapy has been prescribed for patients with positive axillary nodes and has clearly led to prolonged relapse-free survival post-surgery. The benefit of adjuvant systemic therapy in node-negative breast cancer patients, which is greater than 65 percent of all new cases of breast carcinoma, however, is far from clear. Considering the expense and the toxic exposure to the patient, this form of aggressive therapeutic approach is justified only in those who are at the highest risk of relapse. Currently, there is no consensus on how best to identify node-negative patients who have a high risk of recurrence and who are therefore candidates for adjuvant therapy, although this is being actively investigated. To identify a subset of node-negative women who may benefit from adjuvant therapy, additional biomarkers are needed.

THE STUDY OF STRUCTURAL AND NUMERICAL CHROMOSOMAL ABNORMALITIES IN BREAST CANCER USING MOLECULAR CYTOGENETICS

As is true for other cancers, breast tumor cells are often characterized by numerical and structural abnormalities. Whereas structural chromosomal abnormalities are caused by breakage and reunion of chromosomal material leading to translocations, inversions, duplications, deletions, insertions, rings and marker chromosomes, etc., numerical chromosomal abnormalities are caused by nondisjunction. Both structural and numerical chromosomal abnormalities can be studied using the relatively new technique of fluorescent *in situ* hybridization[33,34], described below, as an adjunct to conventional cytogenetic analysis.

To determine whether there is a difference in the prevalence of chromosome aneuploidy in cells from breast cancer patients versus cells from controls, fluorescent *in situ* hybridization (FISH) can be performed using centromere enumeration probes. We are particularly interested in chromosome 8 trisomy (Figure 3), which has been reported in a number of cancers by us and others. Preliminary data on chromosome 8 trisomy and breast cancer have been presented as a platform presentation at the 1995 Annual Meeting of the American College of Medical Genetics in Los Angeles in 1995. A manuscript has since been prepared and has been accepted for publication[35].

FLUORESCENT IN SITU HYBRIDIZATION

It has been said that FISH research[36] is the "most significant research in human genetics." Fluorescent *in situ* hybridization can be used as a measure of genetic instability expressed as aneuploidy. Fluorescent *in situ* hybridization also can be used to detect stable structural rearrangements such as translocations. Using FISH and biotinylated chromosome-specific α-satellite enumeration probes (Oncor, Gaithersburg, MD), numerical chromosomal abnormalities (aneuploidies) can be detected[37-45]. Structural chromosomal abnormalities, on the other hand, can be detected using chromosome-specific painting probes (Gibco BRL/Life Technologies, Inc.; Vysis, formerly Imagenetics, of Framingham, MA; and also Oncor, Gaithersburg, MD[46]. With the latter technique, even complex translocations can be detected (Young, Di Benedetto, Glasser and Mark, manuscript in press). Both techniques are used routinely in our laboratory as an adjunct to GTG-banding.

Other details of FISH (Figure 4) are given in Mark et al[47], Mark[33] and Mark[34]. The last article mentioned provides examples that illustrate the use of the technique in a clinical setting for improved patient care.

For FISH on archival material (see, for example,[39]), two possible procedures can be used for specimen processing. Once slides are prepared, the same basic FISH protocol can be followed.

For hybridization a number of DNA probes can be employed, depending on the specific aneuploidy that one wishes to detect. For our recently published study[35], we employed α-satellite chro-

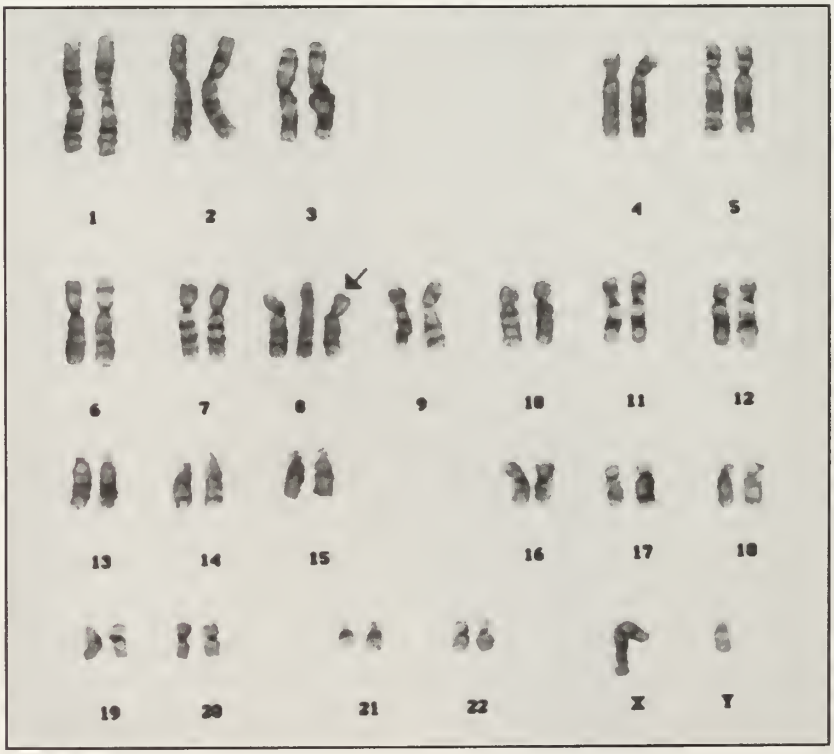


Figure 3. Computer-generated karyotype for illustrating chromosome 8 trisomy. Arrow points to an extra chromosome 8.
(Reprinted with permission from *Rhode Island Medicine*).

mosome-specific probes of chromosome 8. Trisomy for chromosome 8 (Figure 3), the site of the c-myc proto-oncogene, has been reported in a number of cancers as an acquired abnormality, most notably the myelodysplastic syndromes, acute non-lymphocytic leukemia, chronic myeloproliferative disorders, lymphomas, melanomas, sarcomas and choriocarcinomas. It also has been reported in prostate carcinoma[48], ovarian carcinoma[49], salivary gland tumors[50,51], benign nevi[52], colon adenomas[53], gestational trophoblastic disease[54,55] and miscellaneous tumors[56,57]. Fletcher et al[58] suggested that trisomy 8 may be a marker for squamous differentiation in endometrial carcinoma. Trisomy 8 mosaicism also is associated with the Rothmund-Thomson syndrome and Werner syndrome, both of which are characterized by an increased predisposition toward cancer.

Recently, Bullerdiek[59] raised the possibility of trisomy 8 as a recurrent clonal abnormality in breast cancer. These investigators analyzed one benign and 15 malignant breast tumors with a multitude of numerical and structural aberrations but concluded that only trisomy 8 was a recurrent karyotypic abnormality, raising the possibility that trisomy 8 may be an early genetic alteration which characterizes a subtype of ductal breast carcinomas. As an initial step, we plan to test this hypothesis using FISH. Given that trisomy 8 has already been detected in a number of neoplasms mentioned above, it is only logical that its prevalence in breast cancer be investigated.

In our laboratory, the FISH protocol has been successfully performed on fixed cells of peripheral blood, bone marrow, tissue culture of various origin, somatic and radiation hybrid cells, blood smears, bone marrow smears, semen (sperm) smears, cytological specimens, salivary gland tumors, cervical and other cancer cells and cells derived from 20-year-old paraffin sections of gestational trophoblastic disease[54,55].

Pathologic Correlations

To correlate the cytogenetic results with pathological parameters, statistical analyses can be performed. This approach will enable better assessment of the cytogenetic information in the context of the total patient profile routinely obtained as part of the standard protocol. Histopathologic analysis are routinely performed on each specimen to determine tumor type, nuclear grade, vascular/lymphatic invasion, necrosis, mitotic activity, etc. as part of the protocol for evaluating disease aggressiveness. Wherever possible, data on the following prognostic indicators should be gathered for future correlation studies: Estrogen receptor status, progesterone receptor status, DNA ploidy, S phase fraction, HER-2/neu expression, cathepsin D expression, c-myc gene expression, retinoblastoma gene expression, c-fos gene expression, p53 gene expression and gene mutation, Ki-ras gene mutation, HER-2/neu amplification using FISH, c-myc amplification using FISH, p53 deletion using FISH and also estrogen receptor evaluation using FISH. The latter FISH assays have been validated in this laboratory.

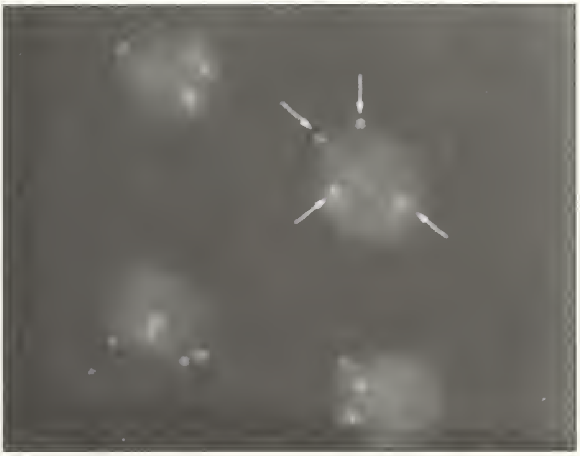


Figure 4. Fluorescent *in situ* hybridization of breast cancer cells.

Conclusion

Currently, the factors associated with tumor initiation, progression, invasion and metastasis as well as the complex relationship between the genetics of breast cancer are not clearly understood. It is known, however, that the risk of developing breast cancer increases with age, family history of breast cancer, and not bearing a child by age 30. Most breast cancer cases (i.e., greater than 70 percent), however, occur in women who have no identifiable risk factors. The basic methods of treatment (e.g., surgery, chemotherapy and radiation) used today are the same as those used in the 1930s. The current criteria for breast cancer staging include pathologic parameters, such as tumor size and nodal involvement, histologic and cytologic parameters, such as histologic grade, and biologic parameters such as age of the patient, hormone (estrogen and progesterone) receptor status, oncogene activation (e.g., c-myc and HER-2/neu) and tumor suppressor gene inactivation (e.g., p53). Although there is evidence that some of these factors may offer some utility in prognosis, the optimal combination of independent prognostic factors remains elusive[60,61]. Thus, the need to explore other potential biomarkers is pressing. Laboratory study of breast cancer using conventional and molecular cytogenetics, together with other forms of analysis, will lead to an improved repertoire of biological markers in the future.

Acknowledgments

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Cytogenetics in Obstetrics and Gynecology

Hon Fong Louie Mark, Ph.D., F.A.C.M.G. and John Lathrop, M.D., F.A.C.O.G.

Cytogenetics is the study of chromosomes. Its power is that it enables the examination of the human genome at a glance (Figure 1). With the advent of the banding techniques in the late 1960's and early 1970's, each chromosome in the human genome, as well as additional deviations from the normal diploid karyotype, can now be distinguished. Thus, the relatively young discipline of human cytogenetics has become an integral part of clinical medicine. It is not surprising then that Medical Genetics, of which Clinical Cytogenetics is a subspecialty, has formally become the 24th specialty under the American Medical Association[1], with the American College of Medical Genetics becoming the professional organization of practicing human geneticists.

In this review, we will discuss the application of cytogenetics in obstetrics and gynecology.

CONVENTIONAL CYTOGENETIC STUDIES

Approximately 15 percent of all pregnancies end in spontaneous abortion. The overall frequency of chromosome abnormalities in spontaneous abortions is at least 50 percent[2]. According to Thompson, McInars and Willard, a chromosome abnormality (usually a structural rearrangement or sex chromosome mosaicism) is seen in one or the other parent in a significant proportion (3-6 percent) of cases in which there have been two successive miscarriages or infertility[2]. In view of the significant contribution of genetic factors in fetal wastage, chromosome analysis has become an option that must be seriously considered in the management of certain pregnancies.

A previous history of birth defects or a family history of numerical or structural chromosomal abnormalities is an indication for chromosome analysis. Other indications include: chromosome studies for women presenting with amenorrhea and pubertal failure, women with chromosome instability syndromes, and those who were exposed to carcinogens or radiation[3,4]. Advanced maternal age is also considered a valid indication. Chromosome analysis can be performed on peripheral blood, amniotic fluid, bone marrow,and other somatic tissues. Germ cell karyotyping, although more labor intensive, is also possible.

Examples of chromosomal abnormalities detected in the practice of obstetrics and gynecology include Turner syndrome, which can be 45,X (~1 in 10,000 females), 46,X,i(Xq) (~1 in 50,000 females) and others such as deletions or mosaics (~1 in 15,000 females). Other chromosomal conditions include trisomy X (~1 in 1000 females), other X chromosome abnormalities (~1 in 3000 females), XY females (~1 in 20,000 females) and 46,XY androgen insensitivity (~ 1 in 20,000 females)[2].

Chromosome analysis is useful for mosaicism detection in phenotypic females with primary amenorrhea, hypergonadotropic hypogonadism and growth retardation with short stature and failure of secondary sexual development. We have recently reported on the detection of the 46,XY cell line in a female patient with 45,X/46,XY mosaicism[5]. This is important because by possession of this cell line the patient is at risk for gonadoblastoma.

Karyotyping is also an invaluable tool in the analysis of gynecologic cancers, such as cervical, uterine and breast cancer. We have also used the techniques of GTG-banding and FISH in the study of gestational trophoblastic disease[6,7].

ABBREVIATIONS USED

ACMG: American College of Medical Genetics
CALGB: Cancer and Leukemia Group B
FDA: Food and Drug Administration
FISH: Fluorescent *in situ* hybridization
GTG-banding: G-banding using trypsin as the proteolytic enzyme treatment and Giemsa as the stain
i(Xq): Isochromosome of the long arm of the X chromosome
NERGG: New England Regional Genetics Group

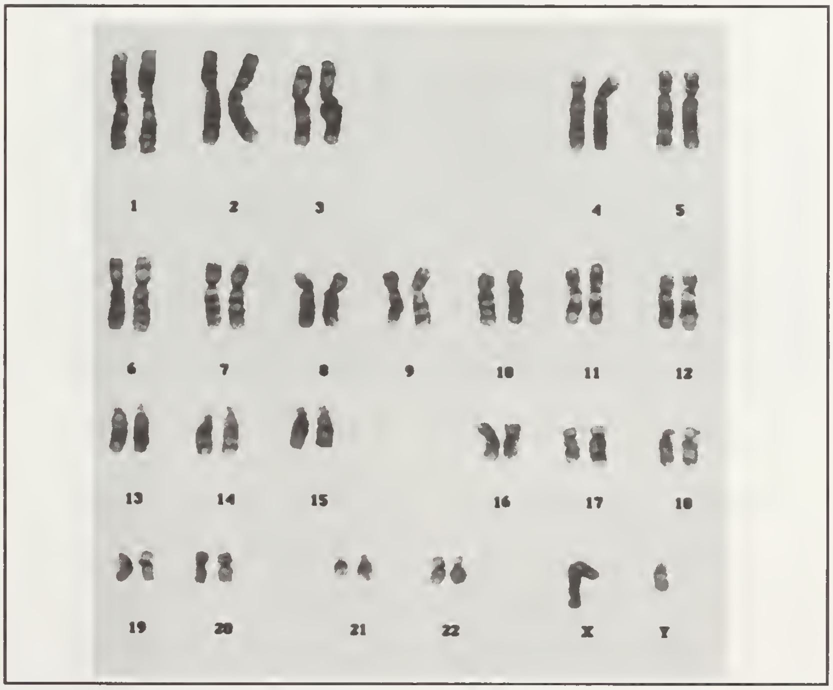

Figure 1. A GTG-banded karyotype. (Reprinted with permission from *Rhode Island Medicine*).

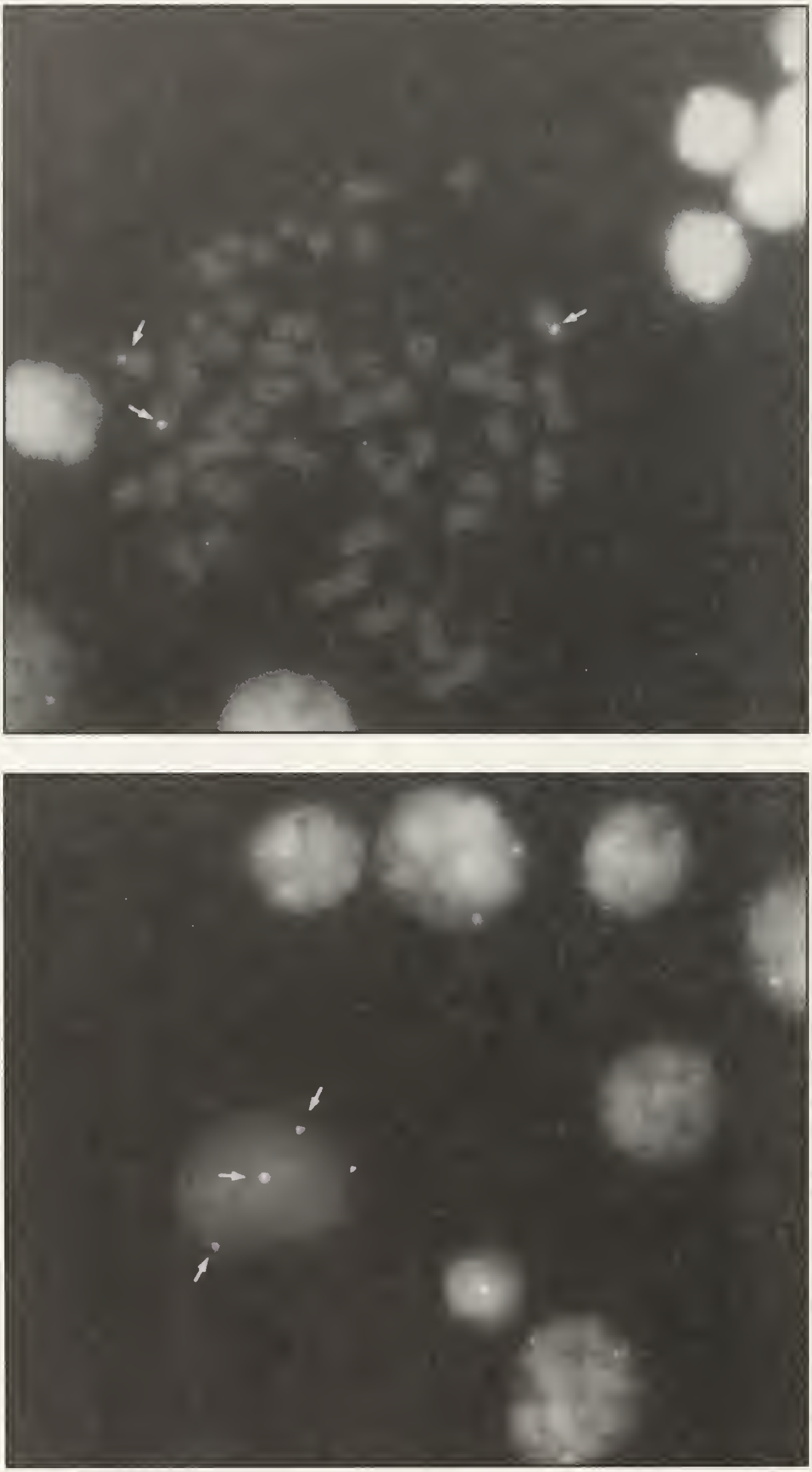

Figure 2. Fluorescent *in situ* hybridization using an α-satellite chromsome 8 specific probe, illustrating chromosome 8 trisomy. (Reprinted with permission from *Rhode Island Medicine*).

NUMERICAL AND STRUCTURAL ABNORMALITIES

Whereas structural chromosomal abnormalities are caused by breakage and reunion of chromosomal material leading to translocations, inversions, duplications, deletions, insertions, rings, and marker chromosomes, numerical chromosomal abnormalities are caused by chromosome nondisjunction. Both structural and numerical chromosomal abnormalities can be studied using the relatively new technique of fluorescent *in situ* hybridization[8,9] (FISH) as an adjunct to conventional cytogenetic analysis.

To detect the presence of chromosome aneuploidy, FISH is performed using centromere enumeration probes. We are particularly interested in chromosome 8 trisomy (Figure 2), which has been reported in a number of cancers by us and others.

Using FISH and biotinylated chromosome-specific α-satellite enumeration probes, numerical chromosomal abnormalities (aneuploidies) can be detected[11,16]. Structural chromosomal abnormalities, on the other hand, can be detected using chromosome-specific painting probes (see, for example,[17]). With the latter technique, even complex translocations can be detected (see, for example,[18]). Both techniques are routinely used in our laboratory as an adjunct to GTG-banding.

An immediate consequence of the ability to assess chromosome copy number in interphase as well as metaphase cells is a potentially larger sample of cells for mosaicism study. A clinically relevant chromosome in which mosaicism detection is important is the Y chromsome. FISH detection of the Y chromosome (and also the X chromosome) is readily achieved. As mentioned previously, this is especially important in a phenotypically female patient where the risk for a gonadoblastoma is increased.

For FISH on archival material (see, for example, [20]), two possible procedures can be used for specimen processing. Once slides are prepared, the same basic FISH protocol can be followed. In our laboratory, the FISH protocol has been successfully performed on fixed cells of peripheral blood, bone marrow, tissue culture of various origin, somatic and radiation hybrid cells, blood smears, bone marrow smears, semen (sperm) smears, cytological specimens, salivary gland tumors, cervical and other cancer cells and cells derived from 20-year-old paraffin sections of gestational trophoblastic disease[6,7]. This last study exemplifies our clinical and research interest in cancer.

GYNECOLOGIC CANCERS

Cytogenetics via GTG-banding and other conventional cytogenetic techniques are established clinical procedures increasingly used in gynecologic oncology. Using GTG-banding, we have been able to detect trisomy 8 mosaicism in a patient with gestational trophoblastic disease. We also have characterized cervical cancer cells in a research setting, in collaboration with Drs. Lundy Braun at Brown University School of Medicine and Dr. Stuart Lauchlan of Women and Infants Hospital[21,22].

For the past two years, we have used the techniques of molecular cytogenetics to study breast cancer, which affects 1 in 8 women. We have prepared a manuscript that has been accepted for publication that outlines preliminary data on chromosome 8 trisomy in breast cancer[23]. An ongoing study aims to confirm and extend the findings of the original study. Evidence thus far indicates that there is indeed a subset of breast cancer characterized by chromosome 8 trisomy.

Toward the development of a cytogenetic research program in the study of breast cancer, we have entered into collaborations with local, regional and national investigators. For example, we have enlisted the help of Dr. Henry T. Lynch as a consultant. We also have taken advantage of the fact that Rhode Island Hospital is a member of the Cancer and Leukemia Group B (CALGB) under the leadership of Dr. Louis Leone and have consulted with CALGB breast cancer experts such as Dr. Ann Thor.

ADDITIONAL COMMENTS

Although conventional cytogenetics via GTG-banding is an accepted clinical technique, FISH is still considered investigational and commercial probes for FISH are not yet FDA-approved. Data based on the use of this technology in a diagnostic setting must be interpreted with caution. The New England Regional Genetics Group[24] recommended that issues of sensitivity, accuracy and applicability need to be addressed more fully before accepting this technology in routine practice. This is also consistent with the recommendations of the American College of Medical Genetics[25], which stated that investigational studies must be distinguished from accepted clinical tests and that this information be clearly given in a qualifying statement.

The best approach is the coordinated use of the newest technology as adjuncts to older, established techniques with strict adherence to quality control and quality assurance guidelines, and the interpretation of results with the utmost caution.

ACKNOWLEDGMENTS

We thank Robin Kiernan for help with the references section of the manuscript. The continued support of Dr. Roger Mark and the dedicated staff of the Laboratory of Cytogenetics, FISH and Genotoxicology, which celebrates its third decade of service also is acknowledged. The breast cancer research discussed in the article was supported in part by a grant from the **American Cancer Society** to Hon Fong L. Mark.

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CREST Presenting with Cardiac Tamponade

Tarek W. Wehbe, MD, Paul Wehbe, MD, Elias Nabbout, MD, and Issam Oneyssi, MD

We report a case of CREST (Calcinosis Reynaud's phenomenon, Esophageal dysmobility, Sclerodactyly, Telangiectasia) that came to our attention because of symptoms of cardiac tamponade. Although many consider CREST a subtype of progressive systemic sclerosis (PSS), our case may shed light on the clinical and pathogenic differences between PSS and CREST.

CREST is regarded as a benign disease that uncommonly involves the internal organs. Our patient with CREST had symptoms of pericardial tamponade on admission. We believe this is the first published description of such an association.

Case Report

A 75-year-old woman was admitted to Faulkner Hospital in Boston for evaluation of diarrhea, abdominal pain and progressive azotemia. She described having Reynaud's phenomenon for the five years prior to admission. This was not associated with any other symptoms of CREST.

On physical examination, her blood pressure was 100/60 mmHg with a baseline of 150/90. She had bilateral basilar lung crackles, severe pitting leg edema and cyanosis with absent pedal pulses. She also had sclerodactyly (but no diffuse scleroderma) and disseminated telangiectasia, which was most pronounced over the face and hands.

> *Are CREST and PSS two different disorders or merely two extreme presentations of the same disease?*

The laboratory tests revealed a blood urea nitrogen of 87 mg/dl and a creatinine of 6 mg/dl. The sedimentation rate was 44mm/hr and the antinuclear antibody titer was 1:2500 with a nucleolar pattern. A chest x-ray showed bilateral basilar fibrosis. Echocardiography showed a large pericardial effusion with evidence of tamponade. The initial diastolic pulmonary artery pressure was 79 mmHg. Her symptoms and renal function improved after pericardiocentesis. Approximately 700 ml of straw-colored fluid was extracted. There was no cytologic evidence of maligancy in the examined pericardial fluid.

Table 1
The Major Differences Between CREST and PSS

Feature	Crest	PSS
10 Year Survival	75%	57%
Demography		
Onset Before 40	50%	36%
Females	83%	73%
Years of symptoms before diagnosis	11.5	4
Non-Caucasians	2%	11%
Organ System Involvement		
Skin	25%	100%
Telangiectasis	8.6%	35.2%
Calcinosis	43%	7%
Reynaud's	95%	86%
Joint Disease	58%	80%
Tendonitis	6%	67%
Myopathy	8%	19%
Esophageal Hypomobility	77%	75%
Serology	-	-
ANA Positivity	48%	54%
Anti-Centromere Antibodies	50%	3%
Anti-Scl 70	17%	38%

A pericardial window was performed after a recurrence of her tamponade. The pathology laboratory reported pericardial fibrosis consistent with a collagen vascular disease.

Thirteen months after her hospital discharge, the patient was alive and well.

Discussion

PSS is characterized by the abnormal deposition of collagen in the dermis of the skin and the vascular bed[1]. Our patient fulfilled the American Rhematism Association's criteria for PSS[2] with sclerodactyly and basilar lung fibrosis. In addition, her Reynaud's phenomenon, telangiectasia and absence of proximal scleroderma satisfy the diagnostic criteria for the CREST variant of PSS.

The unusual feature of this case was the patient's presentation with internal organ involvement, particularly the cardiac tamponade and renal failure. The development of clinically significant internal organ involvement in CREST is usually a late manifestation[3] of this condition. To our knowledge, this is the first published case of CREST presenting with cardiac tamponade.

Myocardial and endocardial lesions in PSS are frequently associated with conduction abnormalities due to foci of myocardial fibrosis. Left ventricular thickening, diastolic dysfunction, and decreased mitral valve closure are also seen in PSS[4]. This patient had none of these features.

Pulmonary hypertension, a feature of CREST, may have contributed to our patient's heart failure, but there was no evidence of this having occurred.

The most interesting and peculiar aspect of this patient's presentation was her early pericardial tamponade. Although pericardial effusion with hemodynamic impairment is not uncommon in PSS, it is quite rare in CREST.

Lewis and Heller found pericardial disease in 7 of 28 patients with PSS examined at autopsy[5]. Matsui reported six such cases in 1924[6]. In a more recent review of the literature, Botstein found that 33 to 72 percent of patients with PSS had pericardial effusion at autopsy[7]. Of these, only 13 percent were recognized antemortem. None of the patients with CREST, however, had pericardial tamponade as a presenting symptom. Ferri et al found that 6 percent of patients with CREST had pericardial effusion but reported no cases with tamponade[8].

The atypical presentation of this patient raises questions about our understanding of CREST and PSS. Are they two different disorders or merely two extreme presentations of the same disease?

CREST and PSS differ in a number of ways (see Table 1). For one, they involve different vessels. Trostel et al found that small and medium-sized renal vessels are involved in PSS, while CREST involves only the smaller vessels[9]. Follansbee et al found that myocardial thallium perfusion is significantly reduced in CREST[10]. Coronary artery disease is found in 28 percent of patients with PSS but is not seen in those with CREST. Second, there is a different pattern of association with other diseases. CREST is associated with an increased risk of pulmonary biliary cirrhosis and pulmonary hypertension, while PSS is not. And third, the autoimmune responses in the two syndromes are directed against different antigens. In CREST, but not in PSS, anti-centomere antibodies are common. Anti-SCl 70 is more common in PSS than in CREST.

This case may shed some light on the relationship between CREST and PSS. It remains to be clarified whether the two are in fact different diseases or CREST is but a subtype of PSS.

ABBREVIATIONS USED

CREST:	Calcinosis, Reynaud's phenomenon, Esophageal dysmobility, Sclerodactyly, and Telangiectasia.
PSS:	Progressive Systemic Sclerosis

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The Licensed Physicians of Rhode Island in the Year 1895

Stanley M. Aronson, MD, MPH, Nikki Deary and Milton W. Hamolsky, MD

Statewide registration of the practicing physicians was first established in Rhode Island about a century ago in the year 1895. In an attempt to generate a profile of these colleagues, one of the authors (MWH) explored the archives stored beneath the State House and recovered the original 466 handwritten applications that had been submitted to the inaugural licensing board during the summer of 1895. The formal document required that the applicant provide the following information: name, place of birth, age, residence, name of medical school attended, year of graduation, graduate hospital training (if any), military service (if any), years practiced in Rhode Island, and type of practice (ie, regular, homeopathic, eclectic, etc.) The completed application, along with a valid medical diploma and the payment of two dollars, then permitted the candidate "to practice medicine and surgery in the State of Rhode Island." The observations summarized below offer a brief profile of these 466 physicians with occasional comparisons to Rhode Island's currently licensed cohort of physicians[1-4].

The applications were all handwritten, and it was the impression of the authors that some of the marginally legible ones must have been hastily completed while in a moving horse-drawn carriage. The permissive spelling in many of the applications also suggested that accuracy in orthography was not a medical school requirement in the years preceding 1895.

BACKGROUND

1895 was a peaceful year. The US population, at 69.9 million, was rapidly expanding largely by virtue of immense numbers of European immigrants. A 59-year-old Grover Cleveland was President and Adlai Stevenson was his Vice President. There were 498,556 people living in Rhode Island. Providence, with a population of 175,597, was a burgeoning international seaport.

As the initial year in which a license was required, 1895 was obviously a time when virtually all Rhode Island practitioners had applied en masse. Figure 1 graphically portrays the numbers of newly licensed physicans, by year, for the 100 year interval of 1895 to 1994. Note the lows in applicant numbers during World Wars I and II. There had been a dramatic rise in new physician applicants in the years beyond 1970, an increase far exceeding the modest rise in general population. Many of these newly licensed represent medical school faculty, both in the clinical and investigative sciences, recruited by Brown University and its affiliated hospitals.

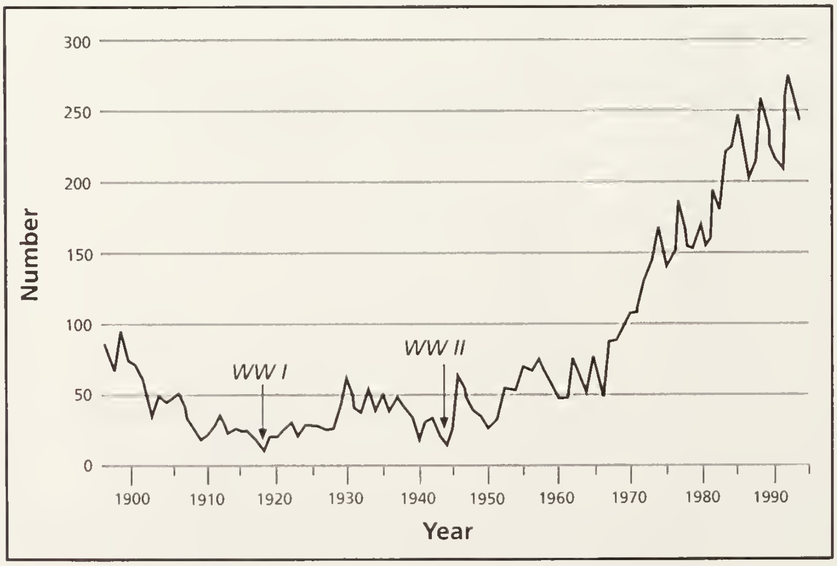

Figure 1. Number of newly licensed physicians, by year (1895–1994).

HISTORICAL PRECEDENTS FOR MEDICAL LICENSURE

Until the early 16th century, the English bishoprics held the responsibility for documenting local persons who provided formal health care. In contrast to the nations of western Europe, Tudor England tolerated little central regulatory activity in deference to what historians called the Anglo-Saxon preference for voluntary, decentralized supervision. Licensing powers were finally bestowed in 1522 upon a secular organization, the Royal College of Physicians, during the reign of Henry VIII; and within two decades the London Company of Barber Surgeons was granted a similar privilege.

The first medical licensing procedure in the Atlantic colonies was enacted by the Massachusetts Bay Colony legislature in the year 1649. It was precedent-setting–but also ineffective[5]. Most practitioners at that time had learned by unregulated apprenticeship or by the recruitment of "native gifts" while many were also practicing clergy. Indeed, English-trained clergy intent on assuming a pulpit in the western Colonies were urged to learn the rudiments of "physick" before departing to the colonies beyond the Atlantic.

Licensure laws, in principle, could regulate professional qualifications, standards of practice, ethical conduct or even fee schedules, but few serious legislative efforts were undertaken to accomplish these ends prior to the current century. Licensure provisions, theoretically, could also formalize an ill-defined profession by creating common standards for all physicians, surgeons and practicing apothecaries; these provisions might even have offered an organizational framework with commonly observed standards, limited membership, and working guidelines between physicians themselves and between physicians and their patients. The Rhode Island Act of 1895 achieved none of these laudable goals, accomplishing little more than the establishment of a statewide registry of those who claimed membership in the medical profession;

Table 1
Physicians Licensed by Rhode Island in 1895

Place of Birth	MD [< 1874]*	MD [1875-89]*	MD [1890 +]*	All
Rhode Island	46	68	42	156
Massachusetts	18	31	18	67
Connecticut	10	15	6	31
Maine	3	13	8	24
Vermont	3	9	3	15
New Hampshire	3	8	2	13
NEW ENGLAND	**83**	**144**	**79**	**306**
	[66.9%]	[66.1%]	[63.7%]	[65.7%]
New York	13	20	3	36
Pennsylvania	4	7	12	23
New Jersey	1	2	1	4
Maryland	1	0	0	1
MIDDLE ATLANTIC	**19**	**29**	**16**	**64**
	[15.3%]	[13.3%]	[12.9%]	[13.7%]
USA, OTHER	4	10	5	19
	[3.2%]	[4.6%]	[4.0%]	[4.1%]
USA, TOTAL	106	183	100	389
	[85.5%]	[83.9%]	[80.6%]	[83.5%]
Canada, Quebec	5	13	9	27
Canada, Maritimes	2	4	2	8
Canada, Other	4	3	2	9
CANADA, TOTAL	**11**	**20**	**13**	**44**
	[8.9%]	[9.2%]	[10.5%]	[9.4%]
Ireland	5	4	0	9
England/Scotland	1	7	3	11
West Europe	1	2	0	3
Southern Europe	0	2	2	4
Eastern Europe	0	0	3	3
Asia	0	0	1	1
Caribbean	0	0	2	2
Non-NORTH AMERICA	**7**	**15**	**11**	**33**
	[5.6%]	[6.9%]	[8.9%]	[7.1%]
Total	**124**	**218**	**124**	**466**

* Physicians receiving MD [or equivalent] degree on or before 1874; between 1875 and 1889; or 1890 or beyond.

nonetheless it began a necessary process which continues today.

Places of Birth

Tables 1 and 2 summarize the places of birth both of the 1895 cohort and the currently licensed group of Rhode Island physicians. Two-thirds of the 1895 group were born in New England, the plurality from Rhode Island (33.5%). Few came from states beyond the mid-Atlantic group. In contrast, the 1995 group of Rhode Island physicians derive from a substantially broader geographic base with more, for example, born overseas (20.1%) than were born in Rhode Island (8.1%). Indeed, in spot-checking places of birth of physicians licensed between 1895 and 1995, it becomes apparent that Rhode Island-born physicians have never at any one time provided more than about 34% of the practicing physicians of this state. Rhode Island, of course, had no local medical school between the years 1831 and 1973 and had persisted as a "debtor" state for most of its existence, relying upon physicians born elsewhere to provide local medical care. Only in recent years has the Rhode Island-born population begun to generate numbers of physicians equal to the medical needs of the state.

When the 1895 physicians are segregated by year of medical school graduation (Table 1) certain additional trends become evident. The fraction born in New England gradually decreases with time while those from more distant states and foreign lands gradually increase. With the younger segment of this 1895 cohort (ie, those obtaining their MD degrees 1890 or later) close to one-fifth (19.4%) were born either in Canada or Europe. The Canadian-born complement of physicians is particularly intriguing since, in 1895, they made up about one-tenth of the entire Rhode Island medical community; most came from the province of Quebec; and after completing their medical studies

Table 2
Places of Birth, 1895 & 1993-4 Cohorts of Rhode Island Physicians

Place of Birth	1895	1993-94
Rhode Island	33.0%	8.3%
New England, including RI	65.7	22.7
Middle Atlantic States	13.7	34.3
USA, other	4.1	21.7
Canada	9.4	1.2
Other	7.1	20.1

had migrated to Rhode Island to serve the immigrant French-Canadian working class communities based principally in the northeast corner of the state.

The overseas-born physicians in 1895 came principally from English-speaking nations and territories (England, Scotland, Ireland, British dependencies in the Caribbean). The overseas-born physicians obtaining Rhode Island licenses in the current decade, on the other hand, stem largely from Asia, particularly India, Pakistan and the Philippines.

AGE AND GENDER

The ages of the physicians under study are summarized in Table 3. The male physicians of the 1895 group, when compared with males currently practicing in Rhode Island, are younger, on average, by 9.2 years. The 1895 physician, on average, was granted the MD degree at age 23.7 years; currently, the figure is 27.6 years. Furthermore a completed internship is now a requirement for Rhode Island licensure and it is a rare physician who doesn't undergo residency training in one discipline or another before requesting a license. In 1895 there was no licensure requirement for any supervised hospital training. Thus, the 9.2 year difference may reflect nothing more than the greater time which the 1995 physicians invest before they enter practice. The small number of women physicians in the 1895 cohort were, on average, older than their 1992 women colleagues. There are hints that many of the 18 women in this group had worked in other fields (nursing, school teaching) before beginning their formal training in medicine.

MEDICAL SCHOOLS ATTENDED

Table 4 summarizes the medical schools attended by the 1895 cohort of practicing physicians. Virtually all currently accredited medical schools in this country are free-standing colleges loosely affiliated with a parent university. Prior to 1895, most functioned as divisions of the parent school rather than as colleges, and were most frequently described as medical departments.

In this 1895 cohort, Harvard Medical School provided more physicians than any other school (74 of the 466 or 15.9%). State University of New York (now called New York University and not to be confused with the current State University of New York) provided 13.3% of the 1895 group of physicians, and Baltimore College of Physicians & Surgeons provided 8.2%. All of the 15 medical schools listed in table 4 were well-established in 1895 and only one (Cleveland Homeopathic) has since ceased operations. Four are still in existence but, through merger or change in ownership, have changed their names. Long Island College Hospital is now State University of NY Downstate Medical School; State University of New York and Bellevue are now merged into New York University

Table 3
Licensed Physicians of Rhode Island: 1895* and 1992** Age Distribution

Age Range	Males 1895	Males 1992	Females 1895	Females 1992
80-89	0	3	0	0
70-79	11	39	0	5
60-69	19	389	0	36
50-59	55	510	6	74
40-49	95	685	6	168
30-39	164	576	6	246
20-29	104	8	0	8
Total	**448**	**2,210**	**18**	**537**
Average Age, yrs	39.5	48.7	45.0	43.1
% below 40 yrs	59.8%	26.4%	33.3%	47.3%
% above 60 yrs	6.7%	19.5%	0.0%	7.6%

* Data derived from current survey

** Data incorporated in reference 4.

Table 4
Licensed Male Physicians of Rhode Island: 1895
U.S. Medical Schools Attended

Graduating on or before 1874 [121]*	Graduating between 1875 and 1889 [209]**	Graduating between 1890 and 1894 [122]***
Harvard [28]	Harvard [33]	P & S, Baltimore [15]
State Univ NY [20]	State Univ NY [32]	Harvard [13]
P & S Columbia [15]	Univ Vermont [16]	State Univ NY [10]
Bellevue [5]	P & S Columbia [14]	Bellevue [9]
Dartmouth [5]	Boston Univ [13]	P & S Columbia [9]
Jefferson [5]	Bellevue [11]	Univ Penn [8]
Univ Vermont [4]	Dartmouth [10]	Boston Univ [7]
Yale [4]	Jefferson [9]	Jefferson [7]
Albany [4]	P & S Baltimore [9]	Univ Vermont [5]
Cleveland Hom [3]	Univ Penn [7]	LI Coll Hosp [4]
LI Coll Hosp [3]	NY Homeopath [6]	Albany [4]
Univ Penn [2]	LI Coll Hosp [4]	Dartmouth [3]

* Number in parentheses is number graduating from named institutions on or before 1874.

** Number in parentheses is number graduating from named institutions between 1875 and 1889.

*** Number in parentheses is number graduating from named institutions between 1890 and 1894.

School of Medicine; Baltimore College of Physicians & Surgeons is now part of the University of Maryland School of Medicine; and New York Homeopathic School is now New York Medical College.

Thirty-seven of the 466 physicians (7.9%) attended US medical schools which have since closed their doors. Some were schools of homeopathic medicine (Boston, Chicago, Detroit) while others, such as the medical schools of Bowdoin College in Maine and Berkshire College in Massachusetts had ceased operations only after years of distinguished service. A few others were short-lived proprietary establishments.

In recent years (1993-95) the medical schools supplying the greatest numbers of current Rhode Island practitioners have been: Brown, Tufts and State University of New York, with its four medical campuses in Brooklyn, Stony Brook, Buffalo and Syracuse[1-4].

Table 5 lists the medical schools attended by the 18 women physicians who were part of the 1895 cohort. Four of the eight listed schools are no longer in existence. Women's Medical College of Philadelphia is still fully operational buty has changed its name to the Medical College of Pennsylvania.

Table 6 lists the foreign medical schools attended by physicians licensed to practice in Rhode Island in 1895. Except for the Canadian-born, all the medical schools were established institutions in central and western Europe.

Of the 466 registered physicians, 77 (16.5%) were not born in the United States. Of the 44 Canadian-born, 22 attended Canadian schools and 22 US schools. In the latter group, most matriculated at the Baltimore College of Physicians and Surgeons suggesting that some historic association may have prevailed between this medical school and Canada. Of the 33 born neither in Canada nor the US, 24 attended US medical schools (presumably they migrated to this country at an early age), while nine received diplomas from seven different European schools.

Except for two Americans attending McGill medical school, none of the US-born physicians in the 1895 cohort received degrees from schools other than those operating in this country. This may indicate the relative ease in obtaining admission to US medical schools during the prior century. Educational prerequisites then were minimal, many schools requiring nothing more than a high school diploma and the ability to pay tuition.

EXAMINATION AS A REQUIREMENT FOR LICENSURE

1895 preceded the Flexner Report –and the stringent educational standards and accreditation procedures generated by it - by 17 years. No nationwide medical school standards prevailed in 1895, and a few schools (eg, the Hygeio-Therapeutic College of New York) were of questionable educational merit. The

Table 5
Licensed Physicians of Rhode Island: 1895
Medical Schools Attended by the 18 Women Physicians

Name of School	No. Attending	School Still in Existence?
NY Women's Infirmary	1	no
Women's Med Coll Philadelphia	5	yes
NY Med Coll for Women	2	no
P & S, Boston	2	no
Boston University	5	yes
Cleveland Homeopathic	1	no
Univ Michigan	1	yes
Tufts	1	yes

Table 6
Licensed Physicians of Rhode Island: 1895 Foreign Medical Schools Attended*

Location	No. Attending
Canadian:	
Victoria	13
Laval	5
McGill	3
Queens	1
European	
Naples	3
Geneva	1
Glasgow	1
Dublin	1
Basel	1
Vienna	1
Paris	1

* In the cohort of physicians licensed in Rhode Island in 1895, none of the US-born attended foreign medical schools. On the other hand, many of the foreign-born attended US medical schools.

Rhode Island licensure regulations in 1895 specified only that the applicant be the lawful possessor of a medical school diploma. It appears, though, that the Secretary of the Rhode Island Medical Board had some latitude in issuing licenses. Occasionally he required that the applicant submit to an oral examination although the criteria for the exercise of such authority was never stipulated. One physician-applicant submitted a letter from his lawyer requesting that the examination be bypassed. The lawyer then declared, in writing, that he would be "glad to reciprocate in the way of such legislation as the Board may desire." The records give no indication as to whether the applicant was required to sit for the examination or whether any *quid pro quo* legislation had been proposed or enacted. The records do indicate, however, that a medical license was indeed granted to this applicant.

Geographic Distribution of Physicians in Rhode Island

The office locations of the 1895 and the 1995 licensed physicians are summarized according to cities and townships in table 7. In 1895 there were 10.4 licensed physicians per 10,000 population; in 1995 there were 26.1 licensed physicians per 10,000 population. In 1895, the distribution was more widespread and evenly dispersed, the lowest in Kent County (8.7 per 10,000) and the highest in Washington County (16.1 per 10,0000. By 1995 the concentration of physicians in Providence County (33.2 per 10,000) was about threefold greater than in Bristol County (11.5/10,000). When the populations of townships and cities are employed as the denominators, the discrepancies in physician-density become even greater. In the city of Providence, the physician-rate is currently 78.5/10,000, while in some townships it is zero. This indicates the likely influence of three factors: Transportation was substantially better in 1995 than in 1895; the state can now easily be traversed in less than an hour and no mainland intrastate site is further than 30 minutes from an acute care hospital. Secondly, the diagnostic and therapeutic equipment of 1995 could no longer be carried in a physician's black bag making necessary the clustering of physicians in or near major clinics and hospitals; and thirdly, a substantial fraction of physicians of Rhode Island in 1995 were deeply involved in medical school or residency training education which requires that their offices were close to the state's centers of undergraduate and graduate education, largely in Providence and Pawtucket.

Because transportation is so much better in the 1990's, most of the smaller communities of Rhode Island can now tolerate the absence of local physicians' offices. In 1895, the greatest ratios of physicians to population were found in the most isolated of the state's communities (eg, New Shoreham, now called Block Island, Little Compton, Charlestown and Westerly). The awesome concentration of physicians in Narragansett (59.1 per 10,000), however, represents an anomaly. Most of the nine physicians registering offices in that community in the 1895 listing were from out of state and practiced in this Rhode Island resort only during summer months.

The concentrations of physicians in Westerly are higher than the state average both in the 1895 and 1995 cohorts. Westerly physicians service a larger catchment area including many adjacent Connecticut communities; the denominator values for this Rhode Island region, hence, are unrealistically low.

Two of the 466 physicians were graduates of the school of medicine of Howard University, a traditionally black institution of higher learning situated in Washington, DC. One of these physicians was born in Bermuda, the other in Barbados. It is possible that these two were the sole African-American physicians practicing in Rhode Island in 1895. One had a prior baccalaureate degree and both had undergone residency training. One established his practice on Cushing St., Providence and the other on Williams St., Newport.

The 154 Rhode Island-born physicians in the 1895 cohort tended to establish their practices within their city or township of birth. Thus, 76% of Providence-born physicians practiced in Providence. Over 80% of Aquidneck Island-born physicians (ie, Newport, Middleboro, Portsmouth) also established offices in the communities of their birth.

The Women Physicians

Eighteen women are included in this 1895 cohort of physicians representing 3.9% of the licensed cadre. They are older than their male colleagues by an average of 4.5 years (Table 3). All attended US medical schools (Table 5) many of which ceased to function shortly after the 1912 Flexner survey. While their formal medical education was undertaken in less well-known institutions, these women entered graduate hospital training to a greater degree than their male colleagues.

Urbanization and the Likelihood of Entering Medicine

In reviewing the 466 applications for medical licensure in 1895, a striking feature is the paucity of non-Rhode Island applicants born in the larger cities of the states of their birth (eg, New York, Philadelphia, Boston, Hartford, New Haven). For example, of the 35 Rhode Island physicians born in the state of New York, only eight came from New York City, while 23 were born in obscure rural villages; of the 67 Massachusetts-born physicians practicing in Rhode Island, only five were born in Boston with the majority coming from

Table 7
Licensed Physicians of Rhode Island: 1895 and 1995: Geographic Distribution

	1895			1995		
Location	Population+	No. MD's	MD's/10,000	Population+	No. MD's	MD's/10,000
BRISTOL CO.	**13,144**	**16**	**12.2**	**48,855**	**56**	**11.5**
Barrington	1,135	2	17.6	15,800	24	15.2
Bristol	6,901	6	8.7	21,734	21	9.7
Warren	5,108	8	15.7	11,321	11	9.7
KENT CO.	**29,876**	**26**	**8.7**	**162,493**	**290**	**17.8**
Coventry	5,279	5	9.5	31,609	8	2.5
E. Greenwich	2,775	5	18.0	11,835	20	16.9
Warwick	21,316	16	7.5	85,823	253	29.5
W. Greenwich	606	0	0	3,963	0	0
W. Warwick*	-	-	-	29,963	9	3.1
NEWPORT CO.	**32,599**	**37**	**11.4**	**86,717**	**114**	**13.1**
Jamestown	1,019	2	18.3	5,249	2	3.8
L. Compton	1,132	4	35.3	3,366	0	0
Middletown	1,457	0	0	18,788	16	8.5
Newport	22,441	25	11.1	27,455	84	30.6
New Shoreham**	1,396	3	21.5	-	-	-
Portsmouth	2,105	2	9.5	17,364	5	2.9
Tiverton	2,977	1	3.4	14,495	7	4.8
PROVIDENCE CO.	**328,683**	**32**	**79.9**	**590,591**	**1,963**	**33.2**
Burrillville	6,317	5	7.9	16,641	8	4.8
Central Falls	18,167	16	8.8	16,167	8	4.9
Cranston	13,343	10	7.5	76,703	167	21.8
Cumberland	8,925	4	4.5	29,727	28	9.4
E. Providence	12,138	7	5.8	50,394	101	17.0
Foster	1,151	1	8.7	4,541	1	2.2
Glocester	1,462	2	13.7	9,441	4	4.2
Johnston	4,305	8	18.6	27,375	47	17.2
Lincoln	8,937	3	3.4	18,546	37	20.0
N. Providence	3,016	0	0	32,287	46	14.2
N. Smithfield	2,422	0	0	10,481	20	19.1
Pawtucket	39,231	32	8.2	71,058	187	26.3
Providence	175,597	208	11.8	155,418	1,220	78.5
Scituate	3,361	3	8.9	9,941	7	7.0
Smithfield	2,107	4	19.0	19,498	7	3.6
Woonsocket	28,204	24	8.5	42,373	75	17.7
WASHINGTON CO.	**24,154**	**39**	**16.1**	**112,688**	**189**	**16.8**
Charlestown	975	2	20.5	6,836	5	7.3
Exeter	841	0	0	5,836	1	1.7
Hopkinton	2,602	2	7.7	7,228	0	0
Narragansett	1,523	9	59.1	15,114	31	20.5
New Shoreham**	-	-	-	874	1	11.4
Kingstown	9,166	8	8.7	49,110	73	14.9
Richmond	1,506	1	6.6	5,603	5	8.9
Westerly	7,541	17	22.5	22,087	73	33.1
Total	**428,556**	**445**	**10.4**	**1,001,344**	**2,612**	**26.1**

+ 1895 population figures derived from U.S Bureau of Census data; 1995 population figures derived from Bureau of Census estimates based on 1990 Census numbers and data on subsequent population trends.

* West Warwick was incorporated as a separate town in 1913.

** New Shoreham (Block Island) transferred from Newport County to Washington County in 1963.RI MD1895

46 different village-sized communities, many close to Rhode Island (Seekonk, Bridgewater, Raynham, Dighton, South Attleboro); and of the 31 Rhode Island physicians born in Connecticut, only two were born in New Haven or Hartford. About half of this Connecticut contingent were born in southeastern townships near the Rhode Island border (North Stonington, East Killingsley, Putnam, Voluntown, Willington). The great majority of physicians in 1895 came from communities barely larger than villages.

Table 8 summarizes the data which pertain to the Rhode Island-born physicians who applied for licensure in 1895. Again, there is an inverse relationship between the size of the township and the number, born in that township, practicing medicine in Rhode Island. In towns smaller than 2,000 the frequency was 19.2/10,000, while in towns/cities larger than 20,000 the figure was 2.3/10,000.

MILITARY EXPERIENCE

Of the Rhode Island physicians graduating medical school on or before 1874, 16.9% served in the US military. Two physicians also served in European armies during the Franco-Prussian War. Of those graduating between 1875 and 1889, 2.3% held military commissions; and of those graduating on or after 1890, the incidence of military experience drops to 1.6%. Many who did serve referred to the Civil War as the War of Rebellion.

FORMAL HOSPITAL TRAINING

Table 9 summarizes the extent of formal post-graduate hospital training undertaken by this cohort of 466 Rhode Island physicians. A variety of names identified them: interne, house officer, hospital steward or supervised assistant. About 29% of licensed physicians listed one or more years of supervised post-graduate hospital training in their licensure applications. With the older group (graduating on or before 1874) this figure was 19.4% rising to 37.9% in the group born at a later date. In the older group, 29.2% of this postgraduate training had been conducted in European hospitals and clinics. This dropped to 4.3% in those graduating after 1890. Nine of the 18 women physicians (50%) listed graduate hospital training, largely in obstetrics, pediatrics or anesthesiology.

UNDERGRADUATE EDUCATION

Only a minority of the 466 Rhode Island physicians (15.7%) had been awarded undergraduate degrees, the majority from Brown University. Possession of a bachelor's degree is associated with an increased likelihood of entering the 19th century equivalent of residency training. Thus, 27.5% of physicians without an undergraduate degree fulfilled some graduate hospital training while 48.5% of those with bachelor's degrees entered graduate hospital training.

CANADIAN TRAINED PHYSICIANS

The Canadian-born physicians practicing in Rhode Island represent two groups distinguishable by language, province of birth and medical school attended. The smaller group, born in the Maritime Provinces, attended US medical schools or McGill University in Montreal. They established their Rhode Island practices largely in Providence or anglophone communities south of Providence. The larger Canadian contingent were derived from Quebec Province, attended the francophone medical schools of Canada (either Victoria or Laval) and virtually all established their practices in communities containing concentrations of French-speaking working class families recently emigrated from eastern Canada to staff the textile mills of the state. Of the 24 physicians registering offices in Woonsocket, for example, 12 (50%) were French-Canadian; in Central Falls, 43.8% were French-Canadian. Other mill-town communities with francophone physicians included Lonsdale, Slatersville, Arctic, Harrisville, Pawtucket and Lincoln. None of the Quebec-born contingent had acquired undergraduate degrees prior to licensure; nor did any avail themselves of graduate hospital training.

The observation offered above that

Table 8

Licensed Physicians of Rhode Island1895

Relationship of Urbanization and Likelihood of Entering Medicine

Size of Township	No. Townships	No.Entering Medicine/10,000 pop.
20,000 +	5	2.3
10,000-19,900	3	2.5
5,000-9,900	8	5.1
2,000-4,900	9	8.5
0 -1,900	12	19.2

County	Population [1895]	No. Entering Medicine	No. Entering Medicine/10,000 pop.
Bristol	13,144	9	6.8
Kent	29,876	15	5.0
Newport	32,599	13	4.0
Providence	328,683	93	2.8
Washington	24,154	24	9.9
Total	**428,556**	**154**	**3.6**

Table 9
Formal Hospital Training
Physicians Newly Licensed in 1895

MD Graduation		No. with Supervised Hospital Training		
Year	No.	in U. S.	in Europe	% Trained
<1874	124	17	4	19.4%
1875-1889	218	54	10	29.4%
1890-1895	124	45	2	37.9%

disproportionate numbers of this cohort of physicians were born in small towns pertains even more strikingly to the physicians born in Quebec Province. All but one came from smaller communities (particularly the towns of St.Rosalio, Ste. Hyacinthe, St. Ours, Vercheres, St. Cuthbert, St. Polycarp, St. Simon and St. Jean Baptiste).

PARALLEL PROFESSIONS

The applicants sometimes volunteered information describing additional professional capabilities. Thirteen of the applicants (2.8%) stated that they were also registered pharmacists. This association of medicine and pharmacy was particularly notable in the physicians who attended medical school in Quebec Province or who were graduates of Baltimore College of Physicians & Surgeons. A few others held concurrent academic posts such as the eminent Charles V. Chapin (applicant number 20) who was also professor of physiology at Brown University and later Director of Health for the City of Providence. Three others had previously held academic appointments in one of the basic sciences before entering the practice of medicine. One physician had been a practicing lawyer; one was an ordained minister, and one a town clerk and probate judge.

TYPE OF PRACTICE

The applicants were asked the following question: "Line of Practice Intended ?" The answers were distributed as follows: "regular" or "allopathic" medicine (83.9%); "homeopathic" medicine (13.1%); "eclectic" medicine (1.1%); "hygienic" medicine (0.2%); while 1.7% left the question unanswered. Very few declared a subspecialty of medicine although two mentioned pathology as a part-time pursuit; one declared that he was a dermatologist, one worked full-time at Butler Hospital, and a few mentioned that their practices would be restricted to eye disease, ENT disorders or obstetrics.

COMMENTS

No systematic search of the local newspapers was undertaken to seek news items regarding these 466 physicians. Nonetheless some anonymous archivist attached an occasional newspaper story, typically unflattering, to the licensee's original application. For example, one physician had been charged with "the fraudulent practice of medicine, quackery and the use of aliases." Despite strongly worded assertions from the New Haven District Attorney detailing these charges, there is no record that his license had been revoked. Another physician was accused of false advertising and his license was removed in 1916. A third physician was accused of performing "criminal abortions." The outcome of this charge was not revealed in the newspaper accounts. Three other physicians were accused of violations of the Harrison Act, of illegal surgery, and of distributing narcotics. Based on a series of "anonymous letters," one physician was accused of providing a fraudulent medical diploma and was alleged to have multiple past convictions for practicing without credentials. Finally, one physician was accused of rape. A newspaper clipping attached to his papers indicated that he was shot years later "by an unknown assailant."

SUMMARY

A brief demographic profile of the 466 physicians applying for licensure in Rhode Island in the year 1895, is presented here. The typical Rhode Island physician of a century ago was a New England-born 39-year-old white male general practitioner who had little undergraduate education, received his medical diploma from an allopathic medical school within 180 miles of his place of birth, typically a small town, had little or no supervised hospital training, professed to no specialty and established his office, often sharing space with his practitioner-father, within the same community in which he was born.

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Public Health Briefings

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Judith Feldman, MD, MPH and John P. Fulton, PhD

Stop Selling Tobacco to Children

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Rhose Island Department of Health
Division of Disease Prevention and Control

The tobacco industry uses its vast advertising resources to recruit replacements for the 1900 Rhode Islanders who die each year because of tobacco use. It is clear to all except the most staunch supporters of the industry that its recruitment efforts yield the greatest results among children. After all, tobacco use statistics have consistently demonstrated that initiation of tobacco use is almost exclusively limited to minors in our society. Regular cigarette smoking may begin for some children as early as elementary school. By the seventh grade, about 6% of Rhode Island children have smoked at least five packs of cigarettes. By the twelfth grade, about 26% have done so.

Although much smoking among children is "experimental," addiction follows for many. Nicotine is one of the most addictive substances known and the inhalation of cigarette smoke is the most efficient means of delivering nicotine to the body. Some authorities have suggested that smoking as few as ten cigarettes may result in measurable addictive effects.

ADDICTING CHILDREN

Statistics from Rhode Island's 1993 Adolescent Substance Abuse Survey[1] clearly demonstrate the inexorable course of addiction among children, from experimenting with cigarettes through regular use. In the seventh grade, only about 4% of school children have smoked as many as 100 cigarettes and continue to smoke. This percentage increases to 8% in the eighth grade, 12% in the ninth grade, 14% in the tenth grade, 17% in the eleventh grade, and 19% in the 12th grade.

As physicians well know, once a person is addicted to nicotine, sustained cessation of tobacco use is extremely difficult. For example, it takes an average of seven years to quit smoking after the smoker has clearly decided to quit. A recent study demonstrated that of many possible determinants of sustained smoking cessation, two of the strongest were being older and having tried to quit smoking a number of times.[2] In short, neither nicorette nor "the patch" nor any other cessation support has proven to be a magic bullet, which is why the best solution to nicotine addiction is to avoid using the substance entirely.

> *Declines in smoking among children began to slow around 1990 and now appear to be reversing.*

MORE BAD NEWS

Recent statistics have demonstrated that the recruitment and addiction of children as cigarette smokers may be increasing in Rhode Island and the US as a whole.[3] Declines in smoking among children achieved largely through anti-tobacco use education in the 1970s and 1980s began to slow around 1990 and now appear to be reversing.

This should be no surprise. In the late 1980s, the tobacco industry intensified cigarette advertising, using techniques that were especially effective with children. "Joe Camel," seen ubiquitously throughout the US on billboards and buses and in magazines and at corner stores became as easily recognized by children as popular cartoon characters on TV. "Marlboro gear" and other promotions of "cool" clothes and accessories began appearing on children's backs and in their pockets despite protestations by tobacco industry spokespersons that these items were "for adults only." What better way to get a teen's attention?

AN OLD BUT GOOD IDEA

Years before "Joe Camel," Rhode Island law prohibited the sale of tobacco to children under 16. The law was amended a few years ago to prohibit sales to 16- and 17-year-olds as well. Similar state laws have been on the books throughout the country for decades. All have been totally ineffective, however, because enforcement, left to the discretion of local police departments, has languished in competition with higher priorities.

The US Congress has recently attempted to remedy this problem by threatening the loss of Substance Abuse Prevention Block Grant funds to states which don't effectively enforce the prohibition of tobacco sales to minors. The "Synar amendment," as this combination of legislation and regulation has come to be known, specifies three conditions for the receipt of full block grant funding: a prohibition of tobacco sales to minors, proof of regular enforcement, and proof that ever-increasing proportions of tobacco vendors comply with the law.

What a wake up call! Acting to comply with the Synar amendment, Rhode Island quickly discovered how easy it was for children to buy cigarettes (the tobacco product most popular among children). In 1994 and 1995 tests of tobacco vendor compliance, about half the vendors approached by underage teens offered to sell them cigarettes. Worse still, underage teens were able to use cigarette vending machines unchallenged almost 9 out of 10 times.

In response, the State has taken two actions. First, as the result of legislation passed by the 1995 Rhode Island General Assembly, all tobacco vending machines in Rhode Island will have to be positioned in the direct line of sight of a responsible person, and will be locked with an electronic device to prevent the sale of tobacco to unauthorized persons. This law took effect January 1, 1996.

Second, the Rhode Island Department of Health, in collaboration with the Substance Abuse Prevention Task Force Association and other community members, has begun working with local Substance Abuse Prevention Task Forces to assure effective enforcement of the law prohibiting tobacco sales to minors.

BUSINESS AS USUAL

The latter effort would have been helped significantly by a bill introduced in the last session of the Rhode Island State Legislature. The bill would have revised the law prohibiting tobacco sales to minors and facilitated its enforcement. The tobacco industry and its allies were able to defeat the bill by arguing that it would be burdensome to Rhode Island business!

Actually, we should thank tobacco industry representatives for clarifying the profits-versus-children's-health issue so forthrightly. Illegal tobacco sales to children is no penny-ante game in Rhode Island. A recent study published in the American Journal of Public Health estimates that illegal tobacco sales to children in our state gross $1.9 million annually.[4]

The fight in the legislature has not ended. The Coalition on Smoking OR Health, whose members include the American Cancer Society, the American Lung Association, and the American Heart Association, will continue to urge the passage of legislation that restricts youth access to tobacco. The tobacco industry and its economic allies will just as assuredly resist all such attempts, despite claims that they have no interest in recruiting children as tobacco users.

LET'S NOT FORGET TAXES

Another strategy that effectively restricts youth access to tobacco is to raise its cost. The easiest way to do that is to raise tobacco taxes, either nationally or locally. The elasticity of cigarette sales in relation to price is about -0.5; a 1.0% increase in price causes a 0.5% decrease in sales. This figure is generally accepted by the tobacco industry and tobacco control advocates, alike, and explains why the tobacco industry resists increases in tobacco taxation as vigorously as it does.

Recent figures from California demonstrate an even stronger effect.[5] Between 1989 (when Proposition 99 raised the California state tax on cigarettes $0.25/pack) and 1992, the elasticity of cigarette sales in relation to the state cigarette **tax alone** (not total price) was about -0.3; a 1.0% increase in tax caused a 0.3% decrease in per capita cigarette sales. The cost increase was about six times stronger than the effect of the anti-smoking media campaign purchased by Proposition 99's cigatette tax dollars!

Rhode Island is no slouch in this arena. Our state has one of the highest cigarette taxes in the nation. Even so, much more could be accomplished with this strategy, as recent statistics on tobacco use among children indicate. Furthermore, as the effect of inflation on the impact of previous tax increases is inexorable, so too must be the tax increases.

THE ROLE OF PHYSICIANS

Physicians are central to the fight against children's addiction. The American Medical Association (AMA) has taken a strong stand in fighting the devious strategies of the tobacco industry.

In July, 1995, AMA leadership ended a tough editorial with these words: "In summary, the evidence is unequivocal—the US public has been duped by the tobacco industry. No right-thinking individual can ignore the evidence. We should all be outraged, and we should force the removal of this scourge from our nation and by doing so set an example for the world. We recognize the serious consequences of this ambition, but the health of our nation is more important than the profits of any single industry. On behalf of the physicians of this country and the people they serve, the AMA pledges its best efforts to the eradication of tobacco-related disease. We solicit the support of the public and our government in this endeavor. It is a worthy cause."[6]

The editorial, which accompanied a four-article, in-depth analysis of "approximately 4000 pages of memoranda, reports, and letters, covering a 30-year period, from the Brown and Williamson Tobacco Corporation," listed 14 recommendations for tobacco control adopted by the AMA leadership (table 1). Among them were two concerning the restriction of youth access to tobacco:

"7. Purchase of tobacco products should be strictly limited to adults, with severe penalties for those who transgress. Underage use of tobacco should carry consequences for the user. All tobacco advertising should be eliminated, and a vigorous counteradvertising campaign should be instituted."

"10. State and federal excise taxes on tobacco products should be increased, both to help defray costs of tobacco-induced diseases and to deter young people from becoming addicted."

In Rhode Island, some physicians have joined the Coalition on Smoking OR Health, Rhode Island Project ASSIST, and their local Substance Abuse Prevention Task Forces to educate the public and its leaders about the need to restrict youth access to tobacco. (Call Ms. Betty Harvey, Rhode Island Department of Health, 277-3293, for more information on any of these groups.)

All physicians should make a point of speaking about the health consequences of tobacco to every school age pediatric patient and every adult patient who uses tobacco. Research has shown that such messages from health providers, if given consistently and relentlessly, are an important motivation for avoiding tobacco or giving it up, once hooked.

Tobacco use is now recognized as the primary cause of preventable chronic disease in the US. Prohibiting the sale of tobacco to children is the single best way to reduce tobacco use and hence, preventable disease. We need every physician in the front lines to defeat this scourge. Even as the tobacco industry is untiring in its efforts to recruit replacement tobacco users, we must be determined to keep tobacco away from children. Together, we can do it.

Table 1
The AMA Position on Tobacco, July 19, 1995

The AMA maintains an unequivocal stance against tobacco. The AMA reminds physicians, the public, and politicians that the damning evidence against tobacco makes opposition to its use a pressing, nonpartisan public health issue. If the industry uses political weapons, so shall we. The AMA will not relent in its opposition to tobacco use.

To accomplish this goal, the AMA recommends and will pursue the following steps:

1. Further efforts should be made to educate physicians, the public, and policymakers about the consequences of tobacco use, the predatory nature of the tobacco industry, and ways individuals can break their addiction to tobacco.
2. Medical schools and research institutions, as well as individual researchers, should refuse any funding from the tobacco industry and its subsidiaries to avoid giving them an appearance of credibility. The B&W (Brown and Williamson) documents affirm our belief that such tobacco industry entities as the Council for Tobacco Research, the Smokeless Tobacco Research Council, and the Center for Indoor Air Research are used by the tobacco industry to convince the public that there still is a controversy about whether tobacco has ill effects, to buy respectability, and to silence universities and researchers. We concur with the recommendation of a subcommittee of the National Cancer Advisory Board that federal funding be withdrawn from cancer research organizations that accept tobacco industry support.
3. Politicians should not accept money from the tobacco industry but should direct their efforts to protection of the nonsmoking majority. Those who do accept money should be identified publicly.
4. The federal Occupational Safety and Health Administration should move forward with its proposal to require smoke-free workplaces nationwide.
5. Local communities should continue to control smoking in public.
6. State legislatures should assume responsibility for ensuring smoke-free areas. Any preemptive tobacco laws should be repealed by public demand.
7. Purchase of tobacco products should be strictly limited to adults, with severe penalties for those who transgress. Underage use of tobacco should carry consequences for the user. All tobacco advertising should be eliminated, and a vigorous counteradvertising campaign should be instituted.
8. The Justice Department should enforce the ban against indirect tobacco advertising such as televised sports events.
9. Tobacco itself should be considered a drug delivery vehicle and placed under the oversight of the Food and Drug Administration, with appropriate regulation as for other life-threatening drugs.
10. State and federal excise taxes on tobacco products should be increased, both to help defray costs of tobacco-induced diseases and to deter young people from becoming addicted.
11. The federal government should prevent the export of tobacco to other countries.
12. The continued contribution to knowledge of the control of tobacco by the National Cancer Institute should be strongly supported.
13. Physicians and the public should support legal action against the tobacco industry to recover billions of dollars in excess medical costs from tobacco-related diseases borne by Medicare, Medicaid, and the Department of Veterans Affairs.
14. All avenues of individual and collective redress should be pursued through the judicial system.

Source: Todd JS, Rennie D, McAfee RE. (Editorial) The Brown and Williamson documents. Where do we go from here? JAMA 1995;274(3):256-25B.

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Health by Numbers

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Jay S. Buechner, PhD, and William J. Waters, Jr., PhD

Oral Cancer in Rhode Island

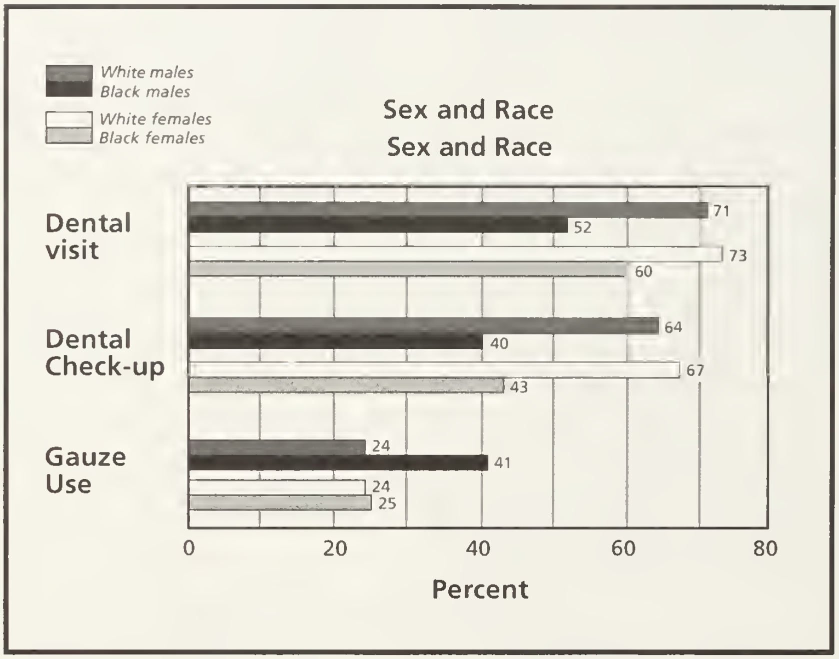
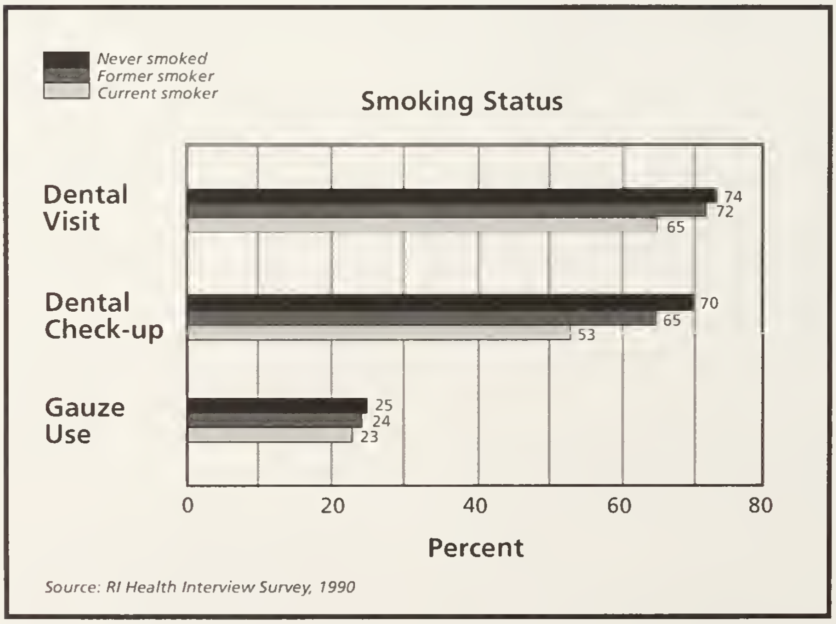


Figure 1. Percentages of adults who reported a dental visit in the past year, who reported a preventive dental check-up and cleaning in the past year, and who reported having their tongues held with gauze during their last dental check-up, by sex and race, Rhode Island, 1990.



Source: RI Health Interview Survey, 1990

Figure 2. Percentages of adults who reported a dental visit in the past year, who reported a preventive dental check-up and cleaning in the past year, and who reported having their tongues held with gauze during their last dental check-up, by smoking status, Rhode Island, 1990.

In anticipation of renewed cancer control planning in the state, the Rhode Island Department of Health analyzed data on oral cancer incidence and mortality for Rhode Island and for the United States, as well as data on oral cancer screening and smoking (a major risk factor for oral cancer[1]) for Rhode Island.

METHODS

State and national incidence rates and national mortality rates were taken from publications of the National Cancer Institute and the North American Association of Central Cancer Registries.[2,3] State mortality rates were constructed from Rhode Island vital records and census data for 1980 and 1990. All rates were age-standardized using the 1970 population of the United States as the standard population. Because previous analysis had suggested underreporting of newly diagnosed oral cancers in Rhode Island,[4] incidence rates for the state were adjusted accordingly. Rhode Island data on smoking, use of dental care, and receipt of screening for oral cancer were obtained from the 1990 Rhode Island Health Interview Survey, a telephone survey of 2,588 households (response rate = 79%) contacted through random digit dialing with over-sampling of black and Hispanic households. Nevertheless, data presented here for Rhode Island's black population are based on small numbers of cases and therefore should be interpreted with due caution.

OBSERVATIONS

An estimated 140 cases of invasive oral cancer are diagnosed annually in Rhode Island. About 40 residents die of the disease each year. Among males, oral cancer incidence and mortality rates for the state are higher than national rates (Table 1). In both the state and the nation, males are far more likely than females, and blacks more likely than whites, to suffer from the disease.

Fewer than three-quarters of Rhode Island adults receive dental care annually, and fewer than two-thirds receive annual dental check-ups (Figures 1 and 2). Only about one-quarter report having had their tongue manipulated with gauze, i.e., being screened for oral cancer, as part of their last dental check-up. This procedure is considered an essential part of thorough oral cancer screening. Whites are more likely than blacks to receive annual dental care, including check-ups. Current smokers are less likely than former smokers and people who never smoked to receive annual dental care, including check-ups.

DISCUSSION

"By 1995, 95% of oral examinations should include a complete tissue screening examination for oral cancer" is one of three screening objectives chosen for Rhode Island in 1989.[5] Baseline data reveal a large gap between this objective and current practice. Data collected in the Rhode Island Health Interview survey to be run in 1996 will measure progress achieved in the intervening years.

Even if the state's oral cancer screening objectives are achieved, however, many Rhode Islanders might not be screened frequently. Only about two-thirds, for example, receive annual dental check-ups, where preventive care focuses entirely on the mouth. This proportion is even lower among groups at higher risk of oral cancer, such as blacks and current smokers.

Primary care physicians can help increase the frequency of complete tissue exams for oral cancer, as recommended previously (Table 2).[5] Complete tissue exams add little time to the cursory oral exams normally performed during medical check-ups, and might be focused on those at high risk of oral cancer. Together, primary care physicians and primary care dentists see a higher proportion of the Rhode Island population annually than either group alone, and might contribute significantly to lowering oral cancer mortality.

Table 1
Incidence and Mortality Rates*, Cancer of the Oral Cavity and Pharynx, by Sex and Race, RI and the U. S., 1988-1991

	Incidence		Mortality	
	R.I.	**U.S.**	**R.I.**	**U.S.**
Males	21.7	16.1	6.2	4.6
Whites	21.0	15.5	6.0	4.2
Blacks	39.2	23.2	11.2	9.4
Females	4.6	6.2	1.3	1.7
Whites	4.6	6.1	1.3	1.6
Blacks	7.0	6.7	2.0	2.3

* Rates expressed as newly diagnosed cases or deaths per 100,000, age-adjusted using the 1970 population of the United States as the standard population. Rhode Island incidence rates have been adjusted for undercount.

Table 2
Screening Recommendations for Oral Cancer

Oral cancer screening should be performed by all health professionals who do oral exams, whenever oral exams are performed, especially on persons 35 years of age and over. Screening should include thorough visual inspection, including extrusion of the tongue with gauze, looking for:

- changes in color (leukoplakia, erythroplakia),
- changes in texture (leathery consistency, strawberry or mulberry appearance),
- changes in continuity (ulcers, lumps), and
- changes in motility (deviations, fixations),

followed by palpation of lips, cheeks, tongue, floor of the mouth, palate, salivary glands and lymph nodes (cervical, preauricular, postauricular), focusing special attention on high-risk areas, including the floor of the mouth, lateral borders of the tongue, hard and soft palate, retromolar trigone area including oropharynx, and documentation of the exam in the patient record. Detection of suspicious lesions should result in prompt treatment or referral.

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Vital Statistics

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Roberta A. Chevoya

Rhode Island Monthly Vital Statistics Report
Provisional Occurrence Data from the Division of Vital Records

Vital Events

	Reporting Period		
	August 1995	12 months Ending with August 1995	
	Number	Number	Rates
Live Births	1,193	13,853	13.9*
Deaths	750	9,696	9.7*
Infant	(15)	(91)	6.6#
Neonatal	(12)	(72)	5.2#
Marriages	836	7,057	7.1*
Divorces	336	3,589	3.6*
Induced Terminations	549	5,834	421.1#
Spontaneous Fetal Deaths	82	1,019	73.6#
Under 20 weeks gestation	(74)	(948)	68.4#
20 + weeks gestation	(8)	(71)	5.1#

* Rates per 1,000 estimated population
# Rates per 1,000 live births

Underlying Cause of Death

	Reporting Period			
	February 1995	12 Months Ending with February 1995		
	Number	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	302	3,263	327.5	4,494.5
Malignant Neoplasms	197	2,409	241.8	7,221.5
Cerebrovascular Diseases	61	590	59.2	702.0
Injuries (Accident/Suicide/Homicide)	22	340	34.1	6961.5
COPD	50	385	38.6	247.5

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.
(b) Rates per 100,000 current estimated population of 996,325.
(c) Years of Potential Life Lost (YPLL).

Note: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

Medicine & Philately

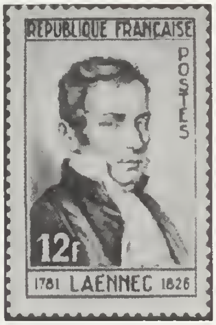
John T. Tierney

Tuberculosis on Stamps

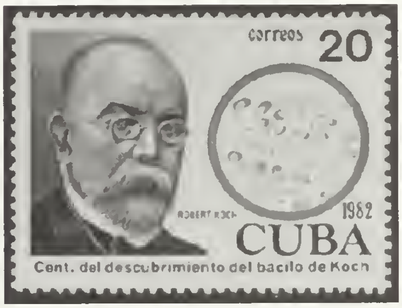
Tuberculosis has been a popular subject in philately. Many countries have honored those scientists who have made major contributions toward the identification, pathogenesis and conquest of the disease. Postage stamps and seals for health education messages also have been widely employed for fundraising for disease control purposes. Because of the current resurgence of tuberculosis, there is now a renewed interest in the disease. The following takes a look at how tuberculosis and other health issues have made their way onto stamps

In 1819, Rene Theophile Hyacinthe Laennec (1781-1826), a French physician and teacher, invented the stethescope, displayed on Japan [Scott 655].* This new medical instrument permitted the presumptive diagnosis of pulmonary tuberculosis by allowing the physician to hear altered breath sounds from within the lungs. Laennec died at age 45 from tuberculosis.

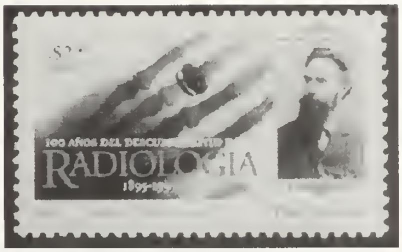
Laennec is honored by France on stamp [Scott 685] seen at right. Verifying the contagious nature of tuberculosis began with the experimental studies undertaken by Colonel Jean-Antoine Villeman (1827-1892), a French army surgeon who demonstrated that the disease could be transmitted by inoculation from one infected animal to another and thus did not arise spontaneously. Villeman is on France [Scott 656].



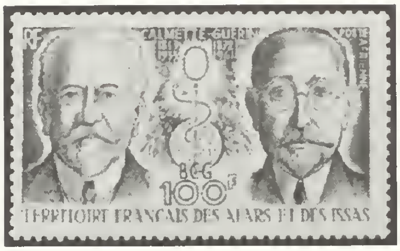
Robert Koch (1843-1910) isolated the *Mycobacterium tuberculosis* in 1882, ending the debate about contagion in tuberculosis. Koch received the Nobel prize for his effort in 1905. He is commemorated on many stamps, including a 1982 Cuban stamp issued to honor the 100th anniversary of the microbial isolation [Scott 626] as seen below. The microscopic field to the right of Koch's face shows the acid-fast nature of the organism.


correos 20
ROBERT KOCH
1982
CUBA
Cent. del descubrimiento del bacilo de Koch

Wilhelm Roentgen (1845-1923) was a German scientist who discovered the nature of x-rays in 1895. His discovery permitted the noninvasive visualization of the chest lesions caused by tuberculosis. He was awarded the Nobel prize in physics in 1901. Roentgen has been honored on a number of stamps, including one from Mexico commemorating the centennial of this discovery, as depicted below.



In 1924, Leon Calmette (1863-1933) and Camille Guerin (1872-1961) collaborated in the development of a vaccine derived from a mycobacterial strain called *Bacillus Calmette-Guerin* or BCG. BCG has been used as a diagnostic aid and as a preventive vaccine, with varying degrees of effectiveness against tuberculosis. These scientists have been honored on many stamps, including one from the Republic of Mali as shown at the top of the next column [Scott 441].


CALMETTE-GUERIN
BCG
100
TERRITOIRE FRANÇAIS DES AFARS ET DES ISSAS

Specific chemotherapeutic therapy for tuberculosis was initiated by the Russian-born American microbiologist Selman Waksman, who discovered and applied the agent streptomycin in 1944. Waksman was awarded the Nobel prize in medicine in 1952 and is commemorated on Gambia [Scott 910].

Numerous other scientists who have made material contributions to the understanding and treatment of tuberculosis also have been honored with portraits on postage stamps. These include: Carlo Forlanini (1847-1918), who introduced pneumothorax for the therapy of tuberculosis and was honored in a stamp of Belgium [Scott B552].

Emily B. Bissell (1861-1948) was a successful advocate for the improvement of children's health services in her native Delaware. Her many accomplishments included the development of free kindergartens, gymnasiums, playgrounds, child health stations, and the organization of Delaware's Children's Bureau. Her cousin, Dr. Joseph Wales, conducted a tuberculosis clinic in Delaware, which was badly in need of funds. He was familiar with the successful effort of Einter Holboell of Denmark, who also operated a tuberculosis clinic, and who had developed the innovative idea of selling Christmas Seals to finance his clinic's operation. Hobell was honored on a Belgium stamp [Scott, B 583]. Dr. Wales then enlisted the help of his extremely effective cousin, Emily Bissell, to establish Christmas Seals, first in Delaware and later throughout the United States. Emily Bissell is honored on a stamp of the United States [Scott US, 1823] with a portrait above the words: "Crusader Against Tuberculosis."

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* *Scott's is an internationally recognized stamp-catalog with a numbering system permitting easy identification. The numbers in brackets are those assigned to the cited philatelic issues.*

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BOOK REVIEW

THE COMPLETE BOOK OF MENOPAUSE
EVERY WOMAN'S GUIDE TO GOOD HEALTH

Carol Landau, Michele G. Cyr and Anne W. Moulton
Published by G.P. Putnam's Sons, New York, 1994

Carol Landau, PhD is a clinical psychologist and Michele G. Cyr, MD and Anne W. Moulton, MD are general internists who are members of the Brown University School of Medicine faculty and founders of the Women's Health Associates, a Rhode Island Hospital-based interdisciplinary practice group. They have coauthored a sensitively written, comprehensive text exploring the many challenges women encounter during their menopausal years.

In each chapter, the reader is provided with information about the natural, normal changes associated with the menopausal years; she then is encouraged and guided to adopt a healthy lifestyle. Hormonal Replacement Therapy (HRT) and the controversy surrounding its use in the control of hot flashes and osteoporosis is well presented. Information is both anecdotal and scientific and abundant references are provided.

The authors stress the importance of recognizing that while menopause does not cause depression, depression can nevertheless affect women during the menopausal interval. When depression is attributed solely to menopause, many women may then not receive the adequate care they need. Above all, the reader is enjoined not to remain isolated when depressive episodes begin.

The overall tone of this book is designed to make the midlife woman aware of some of the problems she and her cohorts may encounter. She is reassured that she is not alone, and she is provided with thoughtful guidelines and sources of help.

This is a remarkably well-written book designed principally for the intelligent woman entering the transitional years of menopause. It is also a valuable and scientifically-sound text which should be read by practicing physicians with patients in this category. The authors have attempted to see women not as the sum of their organs but as full human beings.

Betty E. Aronson, MD

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NINETY YEARS AGO

FEBRUARY, 1906

Herbert Terry, MD describes a recently devised operation for the amelioration of the symptoms of Bright's disease. The procedure consists of the incising or removal of the renal capsule. The author's first reaction: "At first glance this is not an operation that appeals to one. It does not seem good practice to offer such violence to vital organs already diseased ..." He then cites the disappointing work in experimental animals which has not resulted in the hoped-for augmented renal circulation, by anastomosis, to carry on the work of the kidney. Yet, after reflection, Dr. Terry remains impressed with the positive results reported by some observers. Accordingly, he felt justified in recommending the operation to a woman with advanced symptoms including uremia and retinopathy. The operation was performed (and a biopsy from one kidney was interpreted as showing chronic interstitial nephritis). Post-operatively, the patient claimed that she felt substantially improved, although her urinalyses demonstrated no change in their abnormal contents. He concludes that the procedure may perhaps have merit—if performed early in the course of the disease.

The minutes of the Rhode Island Medical Society quarterly meeting at Brown University are published. The yearly fee is raised to five dollars. Twelve new members are inducted while one member, having moved out of the state, becomes a non-resident member. A variety of scientific papers are summarized including presentations exploring dust as a factor in pulmonary disease; the nature of bladder stones; and the present status of surgery of the hypertrophied prostate. A description of the procedure is offered and the observation is made that tuberculosis is not infrequently encountered.

Charles V. Chapin, MD, Superintendent of Health summarizes the mortality rates for October and November of the preceding year. The annual death rate has decreased to 14.57 per thousand, the lowest ever recorded. During these two months, 46 cases of scarlet fever (one death), 77 cases of diphtheria (9 deaths), 43 cases of typhoid (9 deaths) and four deaths from meningitis are reported.

FIFTY YEARS AGO

FEBRUARY, 1946

The lead article, written by O.F.Smith, MD, describes his military and civilian experience with 134 blood transfusions given to 13 separate patients. Reactions to the transfused blood was noted in 5.96% of donations. The author stresses that donor blood of the same type always be used. He concludes that repeated transfusions after short time intervals may be safely undertaken and that whole blood remains the transfusion of choice where whole blood has been lost.

Oral manifestations of systemic disease are discussed by Paul Boyle, DMD. He observes: "The physician is primarily concerned with signs of systemic disease as they manifest themselves in the mouth and with dental infection as it may cause or aggravate disease elsewhere. The dentist looks first of all for something that needs to be repaired. He is in a position to detect early signs of disease which in turn may be called to the attention of the physician to the great advantage of the patient. Progress depends on a greater understanding of the phenomena of disease as manifested in the mouth."

The medical-dental relationship is considered by Albert Midgley, DMD. The author proposes (1) that the problem be surveyed by a committee of representatives from the Rhode Island Dental and Medical Societies, (2) that this committee make a comprehensive study of all available data on the existing relationship and of all suggestions as to what it should be, leading ultimately to a better coordination between individual dentists and physicians in behalf of improved care for the patients of this state.

The mutual obligations and interactions of internists and general surgeons are explored in an article by Thomas Findley, MD.

The lead editorial welcomes the arrival of Oliver G. Pratt as the new superintendent of Rhode Island Hospital.

TWENTY FIVE YEARS AGO

FEBRUARY, 1971

Bertram H. Buxton, Jr, MD, newly elected President of the Providence Medical Society, presents his views on the impending pressures which will be placed upon the practicing physician. He notes: "The practice of medicine, like most arts, is a product of the times. Like most professions, it is ultimately sensitive to multiple pressures, whether they are wrought by advances in applicable scientific knowledge or by society for whom the physicians provide their services." After summarizing the many challenges - and risks - to the integrity of medicine, he concludes: "This is a heated time for medicine. It is a heated time for almost all traditional institutions whether medical, political, social, cultural or economic. If medical practice is to be changed, we the purveyors of medical services must be among the chief cooks."

Charles Hoyt, MD provides a review and overview of the medical problem of alcoholism. "Through the eyes of the alcoholic the physician will slowly gain a different perspective of what is transpiring in the world of the impoverished. He then can't help but be better prepared to face community health issues and their addiction problem that will soon overwhelm us."

Venetia Georas, MD, J.Brian May, MD and Paul LaMarche, MD report on five cases of the Rubinstein-Taybi syndrome.

Robert V. Lewis, MD provides a progress note on the relationship between serum hepatitis and a circulating antigen, demonstrated by complement fixation, called the Australia antigen. While first thought to be an inherited blood antigen, subsequent observations have demonstrated that the antigen is associated commonly with post-transfusion hepatitis and may therefore serve as a diagnostic tool in the detection of this viral disease.

Francesco Ronchese, MD describes two great clinical teachers on the faculty of Padua's medical school: Achille de Giovanni (1837-1916) chief of medicine, and Edoardo Bassini (1844-1924) the chief of surgery.

Editorials discuss the newly established tristate Regional Medical Program, the present status of blood bank screening for viral hepatitis, the continuance of the Framingham study, and progress in the establishment of medical schools in Haifa and Beersheba.

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INFORMATION FOR CONTRIBUTORS

Manuscripts will be accepted for consideration with the understanding that they are original contributions, have never been published in its current form, and are submitted only to *Medicine and Health / Rhode Island.* An article should address a substantive issue of interest to the Rhode Island Medical community. Articles may be no longer than 3,000 words in length and have no more than 20 references.

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Necrology 1995

Vedat F. Akay, MD

Vedat F. Akay, MD, a physician with offices in North Smithfield, and a member of the Rhode Island Medical Society, died September 23, 1995 in Turkey.

Orlando M. Armada, MD

Orlando M. Armada, MD, 76, of Crocus Drive, Cranston, died December 31, 1995 after being struck and killed by a car while crossing Reservoir Avenue. He is survived by his wife, Mary (Geoghegan) Armada.

Born in Havana, Cuba, a son of the late Jose and Julia (Guerra) Armada, he lived in Cranston for many years.

Dr. Armada was a 1946 graduate of the University of Havana Medical School. He came to Rhode Island from Cuba in 1947 and served an internship at Roger Williams Hospital. During his early career, he specialized in pulmonary diseases.

He served in the Army from June 1955 to June 1957 as an assistant chief of communicable disease services at the Brooke Army Medical Center in San Antonio, Texas. Upon his return to Rhode Island, Dr. Armada entered private practice in Providence and later in Cranston, before retiring in 1984. While in private practice, he was on the staff of Roger Williams Hospital.

After retirement, he held consulting positions for the Rhode Island Social Security Disabilities Determination Board and the Rhode Island Department of Health and Human Services.

He received the "Citizen of the Year Award" from the International Institute in 1984. He was a member of the Rhode Island Medical Society, the American Medical Association, and the American College of Chest Physicians. He was a communicant of St. Mark Church.

Besides his wife, he leaves a son, Richard Armada of South Kingstown; three daughters, Dr. Julie Armada of Providence, Ingrid Armada and Diane Greenberg, both of Cranston, and six grandchildren. He was the brother of the late Humerto Armada.

Armand A. Bertini, MD

Armand A. Bertini, MD, 90, of Hastings Avenue, Pawtucket, an orthopedic physician in private practice for many years before retiring in 1975, died January 13, 1995 at the Slater Health Center. He was the husband of Elizabeth (Kinne) Bertini.

Born in Providence, a son of the late Adolfo and Angelina (Giusti) Bertinin, he lived in Pawtucket most of his life.

Dr. Bertini attended Providence College and received his medical degree from Tufts University Medical School in Boston. He was on the staffs of Memorial Hospital, Miriam Hospital, and the former Notre Dame Hospital in Central Falls.

He was a member of the Rhode Island and American Medical Associations, the Pawtucket Medical Association, and the Rhode Island Orthopedic Society. Besides his wife, he leaves a daughter, Elaine Roske of Seekonk, MA; a son, Dr. Richard G. Bertinin, MD, of Pawtucket; five grandchildren and five great-grandchildren.

Sylvester A. Capalbo, MD

Sylvester A. "Cappy" Capalbo, MD, 85, of Edgar Nock Road, North Kingstown, a past president of South County Hospital medical staff, died March 17, 1995 at home. He was the husband of the late Beatrice (Donato) Capalbo.

Born in Bradford, a son of the late Michael and Angelena (Altimano) Capalbo.

Dr. Capalbo was a 1934 graduate of the former Rhode Island State College, now the University of Rhode Island. After receiving a bachelor's degree in science, he attended the Hahnemann Medical College in Philadelphia, PA, and graduated in 1939 with a medical degree. He was a member of the South County Hospital medical staff from 1940 to 1976, and was staff president. He was president of the New England Chapter of the American Cancer Society. He was a county medical examiner. He was a member of the American Medical Association, the Rhode Island Medical Society, the Washington County Medical Society, VFW Post 916, American Legion Post 39, and the South Kingstown Elks. He served in the merchant marine in World War II.

While in college, he held the 1934 pole vault record of 12 feet. He also won letters in football and track, and was inducted into the URI Athletic Hall of Fame in 1988. He participated in the Rhode Island Senior Olympic Games in 1983, and the National Senior Olympics in St. Louis, MO in 1987. He played softball for the "Over the Hill Gang," bowled and golfed until age 83.

He leaves two sons, Kenneth A. Capalbo of Wakefield, and Robert A. Capalbo of North Kingstown; four daughters, Geraldine C. Sloat of North Kingstown, Arlene E. Gould of Concord, NC, Beatrice C. Burns of Wakefield, and Wendy A. Capalbo of Charlestown; three brothers, Nattie Capalbo of Bradford, Orlando Capalbo and Dr. P. Edward Capalbo, both of Westerly; two sisters, Nellie Forsman of Glastonbury, CT, and Julia Picollo of Bradford; 17 grandchildren, and seven great-grandchildren. He was the brother of the late Thomas Capalbo, Angelina Vound, and Athelina Bucci.

Earle F. Cohen, MD

Earle F. Cohen, MD, 75, of 111 Harrison Ave, Newport, owner of the Hotel Viking for the past 19 years, died September 4, 1995 in Newport Hospital. He was the husband of Renee (Ehrick) Cohen.

Born in Providence, a son of the late Dr. Leo Cohen and Etta Cohen, he lived in Newport since 1986. A pediatrician by training, Dr. Cohen led four other lives as well — as an opera impresario, real estate developer, taxpayer advocate, and hotelier/restaurateur.

A graduate of Brown University in 1941, and Tufts Medical School in 1944, he served in the Army during World War II as a medical doctor. He practiced medicine in Providence and Cranston until 1980.

He served on the staffs of Rhode Island Hospital, Miriam Hospital, Roger Williams Hospital, and the Boston Children's Hospital for many years. He was a member of the *Alpha Omega Alpha* Medical Honor Society and the Rhode Island Medical Society. He was the pediatric medical director at the Warwick Neighborhood Health Center for many years.

Dr. Cohen was president of the Rhode Island Taxpayers Action Committee. He was a member of the Temple Beth-El and its Brotherhood. He was a member of the Ledgemont Country Club in Seekonk, and a founding member of the Alpine Country Club in Cranston.

He had been practicing medicine for about 10 years in the 1950s when he began moving into real estate as a builder of homes and apartment houses. He was the founder and president of Custom Builders. He owned the former Millstone Village Inn in North Attleboro, MA. In 1976, he purchased the Viking Hotel in Newport, which is currently operated by his sons, Jon E. and Douglas D. Cohen, both of Newport.

Besides his wife and sons, he leaves a third son, Dr. Eric R. Cohen of Canton, MA, a gastroenterologist; a daughter, Wendy Handler of Chestnut Hill, MA; a sister, Eunice Levine of Little Compton, and four grandchildren.

Frederic W. Easton, III, MD

Frederic W. Easton, III, 71, of Angell Street, Providence, a physician for more than 40 years, died March 27, 1995 at Rhode Island Hospital. He was the husband of Jean (Phillips) Easton.

Born in Pawtucket, a son of the late Frederic W. and Ruth (Horton) Easton, he lived in Providence for many years.

Dr. Easton graduated from Brown University in 1944, and earned his medical degree from Harvard Medical School in 1947. He was a member of the Alpha chapter of Phi Beta Kappa, and was a member of Sigma Chi Fraternity. He was a member of the American College of Physicians, the American Society of Internal Medicine, and the Rhode Island Medical Society. He had a long-term affiliation with the Brown University Health Services.

He was a veteran of the Korean War, and retired as a commander in the Navy Medical Corps Reserve in 1984. He was a member of the Faculty Club at Brown, the Sons of Colonial Wars, and the New England, Massachusetts, and Newport Historical Societies, and the New England Preservation Society. He was a communicant of St. Martin Church.

Besides his wife, he leaves a son, Nicholas

W. Easton of Warwick; three daughters, Meredith E. Mendes of Rehoboth, MA, Heather E. Maypother of Sterling, MA, and Holly E. Harris of Riverside; a stepdaughter, Tracey C. Hurline of Baldwin, MD; three sisters, Martha Lewis Easton of Cranston, Mary Easton Spence of Radnor, PA, and Agnes Frieze McTammany of Foxboro, MA, and four grandchildren.

Alvin G. Gendreau, MD

Alvin G. Gendreau, MD, 68, of Maple Crest Avenue, North Providence, an obstetrician and gynecologist at Women & Infants Hospital, Providence, and St. Joseph Hospital in Providence and North Providence before retiring in 1994, died November 5, 1995 at St. Joseph Hospital in North Providence. He was the husband of Therese M. (Theriault) Gendreau.

Born in Providence, he was a son of the late Alvin A. and Nora B. (Dufresne) Gendreau, and lived in North Providence for many years.

Dr. Gendreau graduated from Providence College and Tufts Medical School. He received his obstetrical and gynecological training at the Margaret Hague Maternity Hospital, Jersey City, NJ, the University of North Carolina at Chapel Hill, NC, and Our Lady of Fatima Hospital, North Providence. While at Women & Infants and Our Lady of Fatima, he was a section chief, and president of the doctors staff, and served on numerous staff committees.

He was a diplomate of the American Board of Obstetrics and Gynecology and a member of the Rhode Island Medical Society, the Boston Obstetrical Society, the *Alpha Omega Alpha* Medical Honor Society, and the Providence College Thomistic Doctor's Guild. Dr. Gendreau was a trustee of Our Lady of Lourdes Church, Providence, where he was a communicant.

Besides his wife, he leaves three sons, Robert G. Gendreau of North Providence, Walter R. Gendreau of Providence, and David E. Gendreau of South Royalton, VT; four daughters, Dorice A. Bucci and Jeannine M. Vallese, both of Providence, Michelle M.Ogilvie of Lincoln, and Anne Marie T. Mikoni of Columbus, OH; a brother, Normand A. Gendreau of North Providence; two sisters, Ella DuBois and Myriel DuBois, both of Inverness, FL, and seven grandchildren. He was the father of the late Normand L. Gendreau.

Francis Edward Hanley, MD

Francis Edward Hanley, MD, 86, of Money Hill Road, Chepachet, a general surgeon since 1952, and chief of radium therapy at Memorial Hospital from 1952 to 1969, died October 13, 1995 at the Bayberry Commons Nursing Home in Pascoag. He was the husband of Gerta (Herdecker-Hadley) Hanley. He was the husband of the late Doris (Dumican) Hanley.

Born in Pawtucket, he was a son of the late Michael and Alice (Oldham) Hanley.

Dr. Hanley graduated from Providence College in 1930 and Georgetown University Medical School in 1934. From 1935 to 1952, he was in general practice in East Providence. In 1942, he became an assistant in radium therapy at Memorial Hospital and also served in the tumor clinic.

During World War II, Dr. Hanley was a medical officer in the Navy from 1944 to 1950. He was the medical examiner for East Providence from 1938 to 1944, public health officer from 1939 to 1944, and a member of the draft board from 1942 to 1944.

Dr. Hanley became senior surgeon in 1952 at Memorial Hospital, where he also served as chief of radium therapy until 1969. From 1976 to 1985, he served at Zambarano Memorial Hospital in the departments of geriatrics, chronic illnesses, and retarded young adults.

Besides his wife, he leaves two sons, Robert F. Hanley of Chepachet and Jeffrey T. Hanley of Jewett City, CT; two daughters, Donna M. Corcoran of Lancaster, PA, and Mary Lou Iamarone of Providence; 17 grandchildren and 18 great-grandchildren. He was the father of the late Francis Edward Hanley, Jr.

Herman Kabat, MD

Herman Kabat, MD, 83, of Saunderstown, died on December 28, 1995 at Rhode Island Hospital. He was the husband of Sarah (Lissitz) Kabat. He practiced medicine for many years in Providence.

Born in Brooklyn, NY, he was the son of the late Sam and Mary Kabat.

A noted physician in the field of physical medicine and rehabilitation, he was an expert in neuromuscular diseases.

He received his PhD at Northwestern University and MD at the University of Minnesota, where he was later a professor in the physiology department. He was a Navy veteran of World War II and held the rank of captain.

His practice began with the field of polio, multiple sclerosis, and spinal cord injuries. He developed a series of rehabilitation hospitals called Kabat-Kaiser Institutes in Washington, DC and California. He relocated to Rhode Island in 1955 when he became the state director of rehabilitation. Later, he specialized in treating lower back pain.

Besides his wife, he leaves a son, David Kabat of Portland, OR; two daughters, Julie Kabat of Albany, NY and Aleix VanZant of Seattle, WA, and five grandchildren.

Harry Marderos Kechijian, MD

Harry Marderos Kechijian, MD, 88, of 33 Dryden Avenue, Providence, a physician and surgeon in private practice for 50 years in Pawtucket and Central Falls before retiring, died January 31, 1995 at the Hallworth House on Benefit Street in Providence. He was the husband of the late Annette Rhéa (Pare) Kechijian.

Born in Providence, he was a son of the late Mardiros and Azniv (Hakimian) Kechijian, who emigrated from Armenia in 1900.

Dr. Kechijian was an honors graduate of Classical High School in Providence. He attended Brown University for two years before his early enrollment in Tufts University School of Medicine, from which he graduated *magna cum laude* in 1929. He commuted daily from Providence to Boston for the four years of his medical studies, then interned at Memorial Hospital in Pawtucket. His offices were on Broad Street in Pawtucket, and later on Clay Street in Central Falls.

He was a member of the American Medical Association, and the Rhode Island, Providence, Pawtucket and Massachusetts Medical Societies. He was a member of the American Society of Anesthesiologists, and a founding member of the American Society of Abdominal Surgeons.

He leaves a son, Dr. Paul Kechijian, a dermatologist in Manhasset, NY, and two grandchildren. He was the brother of the late Natalie Kechijian Jeremiah, MD, Alice Kechijian Bandeian, MD, and Kegham Kechijian, DO.

Edmond C. Laurelli, MD

Edmond C. Laurelli, MD, 91, of Longley Court, Pawtucket, a retired surgeon, died July 7, 1995 at South Bay Manor in South Kingstown. He was the husband of the late Ferdinando (Muccino) Laurelli.

Dr. Laurelli was a member of the medical staffs of Rhode Island Hospital, Memorial Hospital in Pawtucket and St. Joseph Hospital.

He was a 1925 graduate of Brown University and a 1930 graduate of McGill University. Dr. Laurelli was a member of the Rhode Island Medical Society and the American College of Surgeons. He was a retired Navy commander, having served in World War II in the Navy Medical Corps.

He leaves a son, Dr. Henry Laurelli of Wickford; a brother, Fred Laurelli of Warwick and two grandchildren. He was the brother of the late Peter Laurelli.

James R. McKendry, MD

James R. McKendry, MD, 87, of Putnam Pike, Smithfield, chief of orthopedic surgery at Roger Williams Medical Center before retiring in 1975, died June 25, 1995 at St. Joseph Hospital in North Providence. He was the husband of Phyllis L. (Edmond) McKendry.

Born in Philadelphia, PA, a son of the late Andrew and Nellie (Read) McKendry, he lived in Harmony before moving to Greenville two years ago.

Dr. McKendry was a graduate of Hahnemann Medical College in 1930. He moved to Providence and started a practice in orthopedics. He was the physician for the former Rhode Island Reds hockey team. He was a member of the American Medical Association, the American College of Surgeons, and the Rhode Island and Providence Medical Societies. He was an associate member of the International College of Surgeons. He was the US Public Health Surgeon for the Port of Providence.

Besides his wife, he leaves three sons, Dr. James R. McKendry of Augusta, ME, David A. McKendry of Narragansett, and Donald B. McKendry of Maynard, MA; two daughters, Phyllis A. Parker of Raynham, MA, and Mary E. Walker of Syria, VA; 17 grandchildren, and five great-grandchildren.

Robert E. Newhouse, MD

Robert E. Newhouse, MD, 73, of Rocky Hill Road, Scituate, a general surgeon until retiring eight years ago, died March 21, 1995 at home. He was the husband of the late Arlene (Maloney) Newhouse.

Born in Brewer, Maine, a son of the late Horace and Ann-Marie (Keegan) Newhouse, he lived in North Scituate for eight years. He previously lived in Cranston.

Dr. Newhouse graduated from Bowdoin College, Brunswick, ME, in 1942, where he was the captain of the track and cross-country teams. He graduated from Georgetown University School of Medicine, Washington, DC, in 1945, and was a resident in surgery from 1949-1953. He was a medical officer in the Navy in World War II.

He was a member of the surgical staffs of St. Joseph Hospital in both Providence and North Providence, Memorial Hospital, Roger Williams Hospital, and Miriam Hospital, and the former Notre Dame Hospital in Central Falls. He was a past president of the Memorial Hospital of Rhode Island Staff Assistants, and the Pawtucket Medical Association.

Dr. Newhouse was chairman of the quality review committee of the Health Care Review Corporation of Rhode Island. He was a member of the Rhode Island Medical Society, the American Medical Association, and the Providence Surgical Society.

He leaves four sons, Robert Newhouse of Providence, Mark Newhouse of Hopkinton, Richard Newhouse of Charlotte, NC, and John Newhouse of Pinehurst, NC; four daughters, Catherine Bennett of Colorado Springs, CO, Mary Gellman of Hawthorne, CA, Joanne Shoop of Greenridge, MO, and Patricia Dionne of North Scituate; a brother, Carroll Newhouse of Alexandria, VA and 18 grandchildren. He was the companion of Lorraine Desaulniers of North Smithfield.

Marden G. Platt, MD

Marden G. Platt, MD, 90, formerly of Willett Avenue, Riverside, a general practitioner of medicine in Barrington and Riverside for 47 years before retiring, died February 20, 1995 at the East Bay Manor. He was the husband of the late Henrietta E. (Staton) Platt.

Born in Riverside, he was a son of the late Dr. Arthur E. Platt, whom the city of Providence named a school after, and the late Minnie Manchester (Monroe) Platt.

Dr. Platt was a graduate of Moses Brown School in 1922, the University of Vermont in 1926, and the University of Vermont Medical School in 1930.

He was a past secretary of the Rhode Island Chapter of the American Medical Association, and a member of the National American Medical Association for 50 years. He was an Army veteran of World War II.

He leaves a daughter, Darrie-Ann Anderson of Fairfax, VA; a granddaughter and two great grandsons.

Nathan S. Rakatansky, MD

Nathan S. Rakatansky, MD, 87, of 355 Blackstone Blvd, Providence, chief of anesthesiology at Miriam Hospital for 30 years before retiring in 1985, died October 15, 1995 at the hospital. He was the husband of Rachel (Maron) Rakatansky.

A lifelong Providence resident, he was a son of the late Morris and Fannie Rakatansky.

Dr. Rakatansky was a graduate of Tufts University, and completed his studies at Tufts Medical School in 1932. He was an Army veteran of World War II, and served as chief of anesthesiology at McCloskey General Hospital in Temple, TX.

He served on the staff of Miriam Hospital for more than 50 years, and had been president of its medical staff from 1954 to 1955. He previously had a medical office in Providence on Hope Street. He was one of the earliest members of the American Society of Anesthesiology. He was a member of the Rhode Island Medical Society and former chairman of its Impaired Physicians Committee. He was also a member of the American Medical Association and a former president of the Providence Medical Association. He was a member of Temple Beth-El.

Besides his wife, he leaves a son, Dr. Herbert Rakatansky of Providence; two daughters, Sylvia Forman of Providence, and Francee Sugar of New York City; a sister, Belle Kolander of Philadelphia, PA; two brothers, Harold Rakatansky of Providence, and Sydney Rakatansky of Davidson, NC, and nine grandchildren. He was the grandfather of the late Mark Sicher.

James A. Reeves, MD

James A. Reeves, MD, 81, of Tucson, AZ, a retired physician, died August 13, 1995 in Tucson. He was the husband of Adelaide (Sperduti) Thompson-Reeves. He was the husband of the late Thelma (Lander) Reeves.

Born in Norton, MA, a son of the late William and Blanche (Taylor) Reeves, he lived in Cranston until moving to Tucson in 1993.

Dr. Reeves was in private practice in Providence for 31 years, and was affiliated with Roger Williams Hospital, and served a term as chief of staff. He was a 1936 graduate of Brown University and the Hahnemann Medical School in 1940. He was a veteran of World War II and served in the Pacific Theater. He was the physician for the Scandinavian Home for many years. He was a past member of the Warwick Country Club.

Besides his wife, he leaves two stepsons, John A. Thompson of Cranston and Dr. Glenn M. Thompson of Tucson. He was the brother of the late Edythe Reeves.

Stanislawa K. Resnevic, MD

Stanislawa K. Resnevic, MD, 76, of Putnam Pike, Chepachet, died November 4, 1995 at home. She was the wife of Dr. George Resnevic.

Born in Lwow, Poland, she was a daughter of the late Marian and Anna Schubert.

Dr. Resnevic had a medical practice in Chepachet from 1953 until retiring in 1992. She served on the staffs of Roger Williams Hospital in Providence and St. Joseph Hospital in North Providence for many years.

She was a 1947 graduate of the Heidelberg Medical School in Germany, and then moved to this country and served an internship at Harlem Hospital in New York and Memorial Hospital in Pawtucket. She was the vice-president of the Academy of Family Practice and a member of its board of directors. She was a member of the Rhode Island Medical Society and the Amerian Medical Association.

Besides her husband, she leaves two sons, George A. Resnevic, DMD, of Lincoln, and Brian J. Resnevic of Stamford, CT; three sisters, Eugenia Baranowska, Adele Lamberti, both of Columbus, OH, Irene Hrycien of Cranston, and three granddaughters.

Ciro O. Scotti, MD

Ciro O. Scotti, MD, 84, of Hope Street in Providence, a physician with offices in West Warwick from 1939 until his retirement in 1986, died January 23, 1995 at home. He was the husband of Rita Ward (Dwyer) Scotti.

Born in Barano d'Ischia, Italy, a son of the late Dr. Luigi Scotti and Lady Michelina (Iacono) Scotti, he lived in Providence for 50 years.

Dr. Scotti was educated by the Salesian Fathers and the Benedictine monks at Monte Cassino in Italy. He graduated with high honors from the University of Rome Medical School. In Rhode Island, he was on the surgical staff of St. Joseph and Kent County Memorial Hospitals. He was a fellow of the International College of Surgeons, and an associate of the New England Urological Society. He was a member of the American Medical Association and the Rhode Island and Kent County Medical Societies.

He was a knight commander of the Order of St. Gregory, and served as a Palatine Guard during the pontificate of Pope Pius IX. The Capuchin Order of St. Francis granted him its highest award. He was the only American member of FUCI (Federazione Universitaria Cattolica Italiana). For his work in flood relief, he was honored by the City of Florence in 1966.

Dr. Scotti was a communicant of St. Joseph Church, and served as a Eucharistic minister at Miriam Hospital.

Besides his wife, he leaves five sons, Nino D., Francesco M., Peter M., and Joseph M. Scotti, all of Providence, and Ciro M. Scotti of New York; six daughters, Maria S. Chapin, Rita A. and Elena M. Scotti, and Alice M. Mandel, all of New York, Paula S. Shevlin of Bronxville, NY, and Barbara M. Riehle of Washington, DC; a sister, Caterina DiMeglio of Rome; a brother, Salvatore Scotti of Cranston, and 15 grandchildren. He was a nephew of the late Archbishop Giovanni Scotti and Msgr. Ciro Scotti in Rome, and a cousin of the late Msgr. Guiseppi DiMeglio, a canon of St. Peter's in Rome.

Werner Segall, MD

Werner Segall, MD, a physician and member of the Rhode Island Medical Society, died May 23, 1995.

Erwin Siegmund, MD

Erwin Siegmund, MD, 72 of Brandywine Lane, Narragansett, a member of the South County Hospital surgical staff, who also maintained a private practice in Wakefield until retiring in 1988, died February 17, 1995 at South County Hospital. He was the husband of Hona (Bogner) Siegmund.

Born in Debrecen, Hungary, a son of the late Dr. Erwin Siegmund, and Ilona (Weber) Siegmund, he came to this country in 1956, and moved to South County in 1960.

In 1952, he received a medical degree from University Hospital at Debrecen. Dr. Siegmund served a residency at Memorial Hospital in Pawtucket, and joined the South County Hospital staff in 1960. He was also head physician at Camp Fuller in Wakefield for several years, and worked for the University of Rhode Island Health Services. He was a Washington County delegate to the Rhode Island Medical Society.

Besides his wife, he leaves two sons, Laszlo S. Siegmund of Jamestown, and George J. Siegmund of Wakefield; two daughters, Maria M. Duffy of Houston, TX, Klara E. Hahn of Jamestown, and nine grandchildren.

Henry Sprung, MD

Henry Sprung, MD, 83, of Netanya, Israel, formerly of Meschanticut Valley Parkway, Cranston, died October 11 at home. He was the husband of the late Eleanor (Rekant) Sprung.

He was born in Turka, Poland, and had lived in Cranston for several years, moving to Israel last year.

Dr. Sprung practiced medicine for more than 50 years. He last had an office in Providence.

He leaves a daughter, Edie Nadler of Scarsdale, NY; a brother, Baruch Sheffi of Haifa, Israel; and two granddaughters, Lisa and Jessica Nadler, both of Scarsdale.

John Turner, II, MD

John Turner, II, MD, of Medway Place, Providence, a Providence obstetrician and gynecologist for 40 years before retiring in 1988, and associate clinical professor emeritus at Brown University, died December 15, 1995 at Rhode Island Hospital. He was the husband of Elizabeth (Hopper) Turner.

Born in Wayne, PA, a son of the late Warren H. and Harriet T. (Conklin) Turner, he lived in Providence since 1947.

Dr. Turner was educated at Kent School in Connecticut, and received his bachelor's degree from Princeton University in 1940. He earned his doctorate in 1943 at the College of Physicians and Surgeons, Columbia University, New York. He was an associate clinical professor of obstetrics and gynecology at Tufts and Brown Universities. He was a Navy veteran of World War II and the Korean War, attaining the rank of lieutenant commander.

He was on the staffs of Women & Infants and Rhode Island Hospitals. After retirement, he served in the women's clinic at the Veterans Administration Medical Center. He was a member of the American Medical Association, and the Providence and Rhode Island Medical Societies. During the 1970s, he was chairman of District 1 of the American College of Obstetrics and Gynecology, and later served as its vice-president. He was a past president of the Boston Obstetrical Society and the Rhode Island division of the American Cancer Society.

His many memberships included the Hope Club and the Acoxet Club. He was a former member of the Agawam Hunt. He was a senior warden of Grace Church, and a longtime treasurer of the Providence Intown Churches Association.

Besides his wife, he leaves three sons, John Turner III of Claremont, CA, Alexander M. Turner of Arlington, VA, and Stephen C. Turner of Miami, FL; a daughter, Martha W. Turner of Arlington, VA; two brothers, Albert Turner of Cincinnati, OH, and Andrew Turner of Short Hills, NJ; six grandchildren and seven great-grandchildren.

George Turell Van Petten, MD

George Turell Van Petten, MD, 74, of 40 Robin Road, Portsmouth, a surgeon in the US Navy Medical Corps for many years, and also at Newport Hospital for several years before retiring, died December 21, 1995 at home. He was the husband of Grace (Eales) Van Petten.

Born in Champaign, IL, he was a son of the late Robert M. and Inez (Turell) Van Petten.

Dr. Van Petten was a 1942 graduate of Dartmouth College in Hanover, NH. He joined the Navy and was commissioned as an ensign. He was graduated from Washington University Medical School, St. Louis, MO. He did his internship at US Naval Hospital (USNH) in Sampson, NY, and his residency at USNH in Philadelphia from 1948-1954. He was stationed aboard the US Naval Hospital Ship Consolation during the Korean War from 1950-51, and participated in the Inchon Landing and in the Hungnam Evacuation from North Korea.

He returned to Philadelphia to complete his residency, and was then stationed at the US Naval Hospital in Newport as assistant chief of surgery from 1954-59. He was chief of surgery at Yokosuka, Japan from 1959-62, and at Boston Naval Hospital from 1962-65, when he retired as a captain. He received the Presidential Unit Citation from President Truman and the Korean Presidential Unit Citation from Korean President Syngman Rhee.

After retiring, he went into private practice as a general surgeon at Newport Hospital. He was president of the Providence Surgical Society in 1977, and the Newport Hospital Medical Staff from 1979-80. He was a member of the American College of Surgeons, a diplomate of the American Board of Surgery, a member of the Rhode Island Medical Society and the Aquidneck Medical Association. He was a member of the Artillery Company of Newport, and served as a Lt. Colonel and surgeon, having joined in 1973.

Dr. Van Petten served on the board of directors of the Swanhurst Chorus of Newport. He was a member of St. Mary's Episcopal Church of Portsmouth and served on its vestry for more than seven years. He was also a member of the church choir.

Besides his wife, he leaves three sons, Karl H. Van Petten of Middletown, Robert T. Van Petten of Portsmouth, and George E. Van Petten of Middleboro, MA; a sister, Margaret T. Barthelemy of Minneapolis, MN, and four grandchildren.

Jacques Mioni, MD

Jacques Mioni, MD, 79, of Cranston, a physician and practicing psychiatrist before retiring in 1994, died December 10, 1994. He was the husband of Evangelie (Marinis) Mioni who died on March 8, 1995.

Born in Alexandria, Egypt, of Greek descent, he was the son of Isaac and Ines Mioni. Dr. Mioni began his medical career in France, later returning to Alexandria where he established a practice in pediatrics and served as chief of pediatrics at Greek Hospital Th. Cozzika. He met his wife, a nurse, at the hospital and they moved their family to the United States in 1959.

He received his medical degree from the Faculty of Medicine of Paris, France where he was awarded an Externe in Medicine of the Hospital and Civilian Hospices of Paris in 1937, followed by a Diploma of Doctor of Medicine in 1940. Dr. Mioni did his internship at Miriam Hospital, and in 1964, he graduated from the New York School of Psychiatry. He was on the staff of Creedmoor State Hospital in Queens, NY, where he studied with Dr. Lauretta Bender, and at the Drug Addiction Research Unit at Manhattan State Hospital in New York City. Moving to Rhode Island in 1965, he joined the staff of the Rhode Island Medical Center in Cranston. He held a variety of positions there including Clinical Director and retiring as Chief of Psychiatric Services of the General Hospital in 1985. Dr. Mioni also was associated with the Neuro-Psychiatric Institute in Queens, NY, and had a private practice in Manhattan and Jamaica Plains, NY, and later in Providence, where he had admitting privileges at Butler and St. Joseph's Hospitals.

During World War II, Dr. Mioni was a medical officer in the Royal Hellenic Air Force.

Dr. Mioni was board certified in psychiatry. He was appointed to the Commission on Drug Abuse by Governor J. Joseph Garrahy. He was a member of the American Psychiatric Association, Rhode Island District Branch of the American Psychiatric Association, Rhode Island Society of Neurology and Psychiatry, American Medical Association, Rhode Island Medical Society, Providence Medical Society and the Society for Adolescent Psychiatry.

Dr. Mioni leaves a son, Sotiris Mioni of Cranston; a daughter, Myrto Mioni Morrissey, who is married to Kenneth J. Morrissey, MD, of Cranston, and two grandchildren, Stephen and Melissa Morrissey.

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COMMENTARIES

Update in Selected Subspecialties of Internal Medicine

This year's update includes reviews in the fields of infectious diseases, HIV and AIDS, pulmonary medicine, oncology, endocrinology/metabolism, nephrology and cardiology. Because of space limitations, some the manuscripts will appear in this issue and others in May. Authors were instructed to review recent and significant advances in their respective fields that have particular appeal to the practicing physician. By following these guidelines, some areas of emphasis were included in several articles. For example, it is clear that molecular biology and molecular genetics have had an important effect, not only in the basic science laboratory, but as diagnostic and therapeutic tools that are being used by many generalist and specialist physicians throughout the United States.

Common Themes

Drs. Opal and Flanigan and co-workers discuss the importance of molecular and immunologic events in pathogenesis, diagnosis, and treatment of HIV disease. Multi-drug resistant tuberculosis, as a scientific and clinical challenge, is presented by these authors as well as by Dr. Passero in "Recent Advances in Pulmonary Medicine." Dr. Passero also reviews the use of gene therapy as a treatment for cystic fibrosis. In the area of oncology, Dr. Sikov succinctly discusses the importance of programmed cell death (apoptosis) as it relates to the *bcl-2* and *p53* gene in the diagnosis and treatment of cancer. Similarly, the inherited cancer syndromes and their molecular genetic underpinnings are reviewed. The importance of psychological, ethical, and legal implications of identifying "at risk individuals" is also touched upon by Dr. Sikov.

Other subject areas overlap as well. The importance of diabetes control, complications trial and the use of ACE inhibitors in diabetic renal disease are discussed by the authors of the nephrology article in this issue, and the endocrinology article which will appear in May.

Specific Reviews

Dr. Opal's infectious diseases review contains useful information regarding emerging pathogens and problems with familiar organisms that have become drug resistant.

Dr. Passero's pulmonary review also touches upon newer views about common diseases including asthma, pulmonary embolism, sleep apnea, the hepatopulmonary syndrome, COPD and other important areas dealing with mechanical respirators and air pollution.

In addition to molecular data, the review by Dr. Sikov contains helpful information about newer chemotherapeutic agents, including the mechanisms of biologic agents that have recently begun to be used. In addition, he provides empiric observations about the utility of simpler and standard chemotherapy for the lymphomas.

Drs. Maher and Dworkin, authors of the nephrology review, discuss attempts to intervene in acute renal failure, methods to avoid contrast-induced nephropathy and the important field of diabetic nephropathy and its prevention. The role of diet in renal failure, the treatment of hypertension and its potential to prevent adverse cerebrovascular and cardiac events, and new angiotensin II receptor antagonists also are reviewed.

The readers of these reviews may be startled and challenged by the basic science addressed, but gratified by the realization that steady progress continues to be made. The evidence of such progress is best realized when the clinician understands and exploits molecular and immunologic events at bedside for the benefit of the patient.

Fred J. Schiffman, MD

The Many Faces of Aphrodite

Until recently, infections such as gonorrhea or syphilis were referred to, customarily in whispers, as venereal disease (VD). The term has since been supplanted by a more neutral phrase, sexually transmitted disease (STD), partially for its greater explicitness and partially to avoid a tacit form of sexism embedded in the former name. The word, venereal, is derived from the Latin, *veneris*, meaning to adore or love, particularly in a sexual manner; and at a deeper level it is rooted in the name, Venus, the Roman goddess of love. Calling a disease venereal, (ie, naming it after the female partner) implies therefore that the principal wellspring of infection emanates from the woman. This unstated presumption ignores the epidemiologic reality that the source for contracting an STD may be either the male or the female.

The brightest star in the firmament, the evening star, was called Venus by the Romans. Both its brilliance and its regularity of heavenly transit caused it to be readily incorporated into the ritual beliefs of numerous cultures, particularly as the celestial representation of generative force and renewal. Nomadic peoples also regarded it as the heavenly shepherd guiding the flocks of lesser stars. The Mayan calendar was based on the Venusian cycle. Quetzacoatl —their name for Venus —appears as an evening star for a while, disappears for an interval and then reappears as the morning star. In Mayan and other cultures, hence, it becomes the star signifying death and rebirth and an important astral symbol of fertility. Astrologically it was said to be endowed with the womanly qualities of sensory appreciation, love and pleasure. (Despite our denying any influence exerted by the stars, it is odd that so many currently used behavioral adjectives are derivatives of planetary names: thus we have persons whose nature might be variously called mercurial, martial, earthy, saturnine, jovial —or even venereal.)

The Sumerians taught that this luminous planet was the daughter of the moon, patroness of evening pleasure and hence intimately associated with their rites of temple prostitution. This bright evening star was closely affiliated with their goddess of fertility called Ashtarte by the Phoenicians and Ishtar by the Assyrians. Frazer[1], in describing the transition of a fertility goddess to her widespread pre-Christian status as protectress of harlotry, observes:

"...*we may conclude that a great Mother Goddess, the personification of all the reproductive energies of nature, was worshipped under different names but with a substantial similarity of myth and ritual by many peoples of Western Asia*."

He elaborates further on this:

"*At Heliopolis or Baalbec in Syria, famous for the imposing grandeur of its ruined temples, the custom of the country required that every maiden should prostitute herself to a stranger at the temple of Astarte, and matrons as well as maids testified their devotion to the goddess in the same manner. The emperor Constantine abolished the custom, destroying the temple, and built a church in its stead.*"

As the territory of Grecian influence expanded, their panoply of gods and goddesses comfortably embraced myths hitherto confined to the Middle East, including the many stories concerning Astarte who was transformed, in Greek, to Aphrodite. The Greek word, *aphros* means foam and relates to the prevailing myth of Aphrodite's birth rising fully formed on a scallop shell from the foam of the ocean (as portrayed by Botticelli.) Hesiod, in *Theogony*, provides the grim clinical details: When Uranus was castrated by his son Cronos, the severed organ and its seed was cast into the ocean depths from whence arose the Erinyes (the Furies) as well as Aphrodite. She was said to represent a spectrum of loves from the most sacred to the most abjectly profane. By all who worshipped her she was called Aphrodite *anadyoneme* (born of the sea); by those seeking a fertile marriage, Aphrodite *genetrix* ; for those pursuing spiritual love, Aphrodite *urania* (Urania, the muse of astronomy, from the Greek meaning heavenly); and finally those engaged primarily by lust, Aphrodite *porne* (Greek, meaning harlot.) Aphrodite's several assignments, however, were not evenly distributed amongst her various earthly representations: her role in furthering procreation became negligible while, in the minds of most, she evolved as the symbol of physical love and insatiable sexual excess. Her promiscuity was legion and her consorts included Poseidon, Ares, Hermes, Dionysis and uncounted mortals. One of her many offspring was Aeneus later the founder of Rome. And potions said to enhance physical desire, for example, were called aphrodisiacs.

The word, venerate, (to worship, to revere) is similarly derived from the Latin, *veneris*, and hence it is curious that "venerable" should end up defining prelates and scholarly professors while "venereal" narrowly portrays base diseases customarily associated with prostitution. Perhaps this etymological divergency is reflected best in the sin-

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gular, but contradictory, attributes of Aphrodite who as but one goddess was both venerated and considered venereal.

Following the ascendancy of Rome, many elements of the Greek pantheon were absorbed, with their names altered but their lineage, deeds and misdeeds scrupulously preserved. Thus Hermes became Mercury, Athene evolved into Minerva—and Aphrodite, with her magic girdle, became Venus. Aphrodite's dalliances, affairs and infidelities, however, were perpetuated in the borrowed mythology which surrounds Venus.

The word, venereal, describing that form of love based solely on lust, appears in secular English texts by the 16th century and by the 17th century a family of diseases (called venereal distempers) describes such disorders as French Pox (ie, syphilis.) By 1865, some of the English medical texts talk vaguely about a venereal virus. These same texts make it clear that gonorrhea was endemic; and in Victorian times was considered by men as a moral blemish but also as proof of manhood. Syphilis, the other major pillar of 19th century venereal distemper, was also widespread, reaching from the ghetto occupants of 19th century London to some of England's leading statesmen.

Special amongst the family of infectious disease are those transmitted by sexual intimacy: Special because of the narrow range of activities which facilitate the transfer of the pathogen; and special because of the revulsion with which they have been historically regarded. Certainly no category of human disease has been so roundly condemned or has caused to be created so many euphemisms, paraphrasings and synonyms. And as long as "venereal" carries a faint whisper that women are the prime reservoirs and generators of sexually transmitted diseases, the word should be jettisoned as a diagnostic term to join such discards as Mongolian Idiocy and Gargoylism.

Stanley M. Aronson, MD

Reference

1. Frazer, JG. *The Golden Bough*. London: MacMillan; 1922.

The Ascendancy of the Middle Name

In early biblical times, a single name seemed adequate to identify each person. But as the post-diluvial populations swelled, occasional name-modifiers were added to distinguish one person from another (eg, Elkanah, son of Jeroham; Esther, daughter of Mordecai; Nahash the Ammonite). The world became increasingly complex and inevitably the numbers of people needing distinctive names exceeded the numbers of single names. Wills now required precision in the naming of recipients; contracts demanded accurate names; and courts of law no longer tolerated onamastic ambiguity. A binomial system, requiring both a family and a given name, gradually evolved in the Western world.

What information should a person's name provide beyond the minimum necessary for unmistakable identification? If specificity alone were needed, a numeral by itself would suffice(as virtually all the armies of the world have long since discovered.) Demographers estimate that the total number of humans since the species evolved has not yet exceeded 40 billion which means that we can comfortably identify each person, past, present and near future, with a unique eleven-digit number. But names offer more than mere identity. They hint at lineage, family occupations, ethnicity and geographic origins; they tell us, sometimes, which clan we came from; they recall great deeds of the past; and they tell us our father's family name. A fascination with our ancestry, based almost solely on lineage traced through family names, has created the vast cottage industry of genealogy.

Knowing the family name, however, provides us with the identity of only one half of our ancestry. The maternal family names are customarily lost in those cultures observing a pure system of patrilineage. By the development of a middle name system, however, a mechanism became available by which the mother's lineage might be preserved. Spanish speaking cultures place the maternal name last while the family name (ie, the father's name) assumes the middle position, often with an intervening hyphen. Some Iberians believe that a hyphenated last name adds a touch of aristocracy because it makes clear that both maternal and paternal ancestors were clearly identified and duly recorded in baptismal archives. The greatest of all Spanish scientists, Don Santiago Ramon-y-Cajal, might have been addressed as Don Santiago or as Senor Ramon-y-Cajal since both lineage names became, in a sense, a fused patronymic.

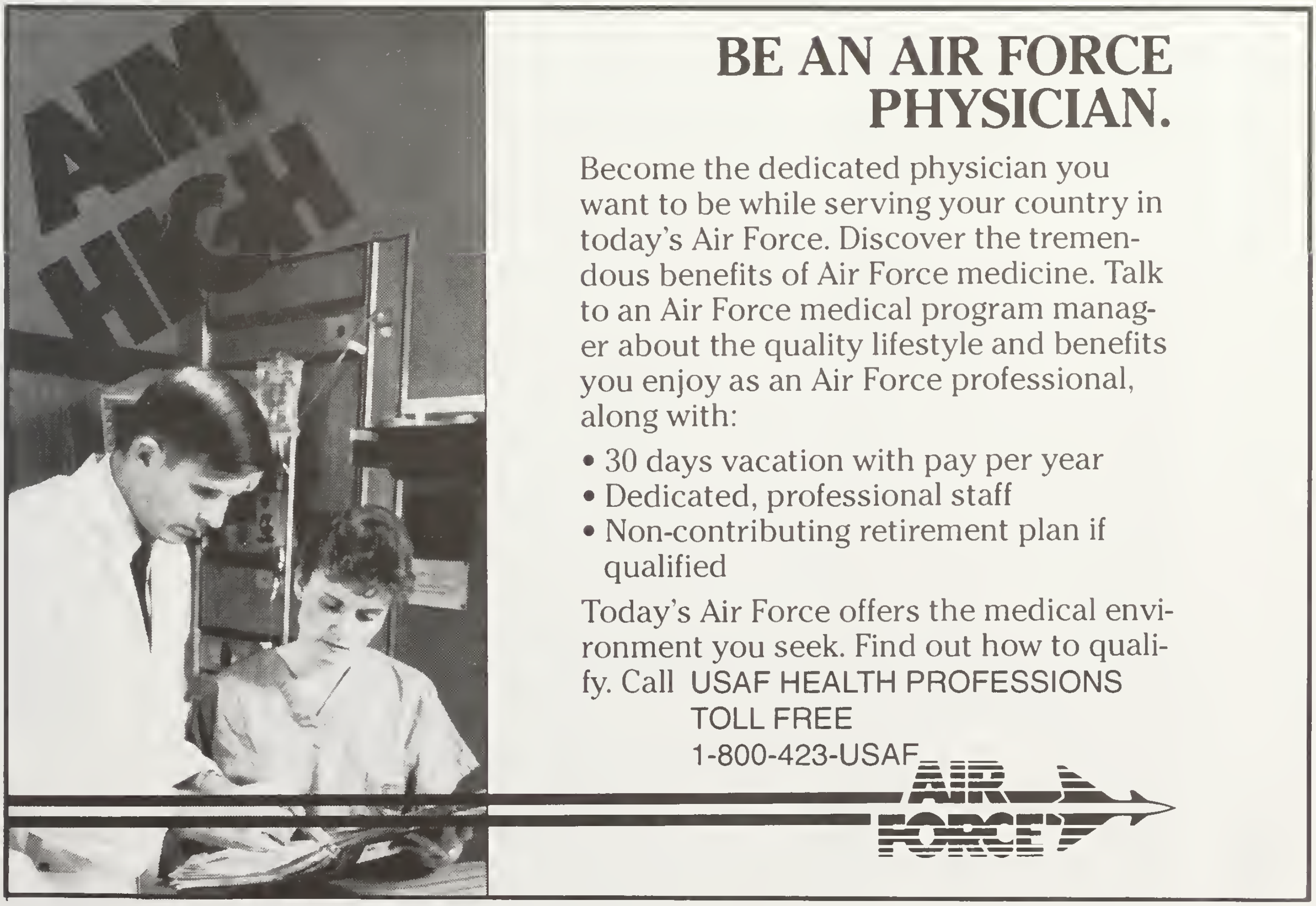
In the English-speaking world, the maternal family names were treated much like recessive genes—hidden in the shadows of the dominant patronym. The English then devised their own system of adopting the maternal surname as the new middle name, indeed, often emphasizing it. Take, for example, some of the eminent 19th century British writers: William Makepeace Thackeray, William Butler Yeats, Elizabeth Barrett Browning, Joseph Rudyard Kipling, Arthur Conan Doyle (none of them would be instantly recognizable without their middle names. Does, for example, Arthur Doyle or Joe Kipling produce immediate name-recognition?). And their American counterparts of British ancestry: Henry Wadsworth Longfellow, James Fenimore Cooper, Edgar Allen Poe, John Greenleaf Whittier and Oliver Wendell Holmes. What reader would readily recognize an author named Ed Poe or Ollie Holmes? The middle name, for many, has therefore become an inseparable, even essential segment of the family name to the extent that both names are linked in oral discourse. We speak readily of Lloyd George, or Foster Dulles or Cabot Lodge as though there were a hyphen welding the middle and last names. This middle name assumes such prominence that it is taken to be, and often becomes, the person's first name (eg, Claiborne Pell, Rudyard Kipling.)

The persistent attachment of the middle name, while endearing, can also be confusing. A problem arises particularly with eponymic tests, signs and syndromes of medical significance. Thus, for example, we have Stokes Adams, Brown Sequard, Foster Kennedy, Cheyne Stokes, Marcus Gunn, Bence Jones, Ramsay Hunt, Guillain Barre and Argyll Robertson phenomena. Which of these represent a partnership of two contributors and which the efforts of but one physician burdened with a domineering middle name?

John Cheyne (1777–1836), Robert Adams (1791–1815) and William Stokes (1804–1878) were three entirely separate physicians whose various observations intersected, allowing others to append their names to syndromes. Georges Guillain (1876–1961) and Jean Barre (1880–1969) were French clinicians. On the other hand, Brown Sequard (1817–1894), born as Edouard Brown, had later adopted his mother's maiden name, Sequard, long before he had visions of neurophysiologic immortality. Robert Foster Kennedy (1884–1952), the great American neurologist, was but a single person. Certainly he could never have anticipated that another Robert Kennedy might preempt the name and that the Foster linkage helped to preserve his more modest identity. Robert Marcus Gunn (1850–1909) was an eminent British ophthalmologist. Henry Bence Jones (1814–1873) was a well known London internist. (In the leading medical dictionaries, he is listed primarily under the letter "B.") And James Ramsay Hunt (1872–1957) was an American neurologist.

And finally, on this brief list, we have Argyll Robertson (1837–1909) the eminent Scottish ophthalmologist. His complete name was Douglas Moray Cooper Lamb Argyll Robertson, an awesome name designed to honor even the most remote of maternal branches within the family tree. Robertson's 1869 paper, his visa to a deathless reputation, described a pupil insensitive to light while pupillary response to accomodation remained unimpaired. He noted this dissociative phenomenon in four patients with degenerative spinal disease (tabes dorsalis.) Why Robertson selected Argyll rather than any of the others as his chosen middle name remains a minor mystery. While touring Gondahl, India, Robertson unexpectedly died. In his day, he was Scotland's leading eye surgeon and an outstanding teacher of ophthalmology. One of his colleagues once observed: "It is better to be an Argyll Robertson pupil than to have one."

Stanley M. Aronson, MD



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Recent Advances in Medical Oncology — 1995-1996

William M. Sikov, MD

Over the last few years discoveries in a number of fields have raised hopes that major advances in the treatment and prevention of neoplastic diseases may be imminent. In some cases, the advances have come in areas familiar to medical oncologists, such as the introduction of new classes of chemotherapeutic agents. Others have come in less familiar areas, such as the expanding role of biologic agents in the treatment of certain malignancies. Advances in our understanding of factors that control cell proliferation and death in normal and malignant cells may lead to new approaches to cancer prevention and treatment. The identification of genes responsible for inherited tendencies to develop one or more cancers holds promise to advance our understanding of the etiology of sporadic cancer as well. However, the failure of well designed studies to confirm some "great treatment advances" cautions us to retain a healthy skepticism when evaluating promising, but preliminary results.

In the following pages, recent advances in medical oncology and allied disciplines are discussed. While many of these advances have little effect on the treatment of patients being seen by medical oncologists today, they are likely to affect our approach to neoplastic diseases within the next decade.

NEW CHEMOTHERAPEUTIC AGENTS

Paclitaxel (Taxol) was identified as the active constituent in a crude extract from the bark of the Pacific yew tree (*taxus brevifolia*) that demonstrated significant cytotoxic activity against a wide range of malignant cells in culture. Problems with supply and solubility of the drug and a high incidence of acute hypersensitivity reactions seen during initial clinical trials were eventually solved. Investigators were encouraged by the drug's broad spectrum of anti-tumor activity in the laboratory and its novel mechanism of action.[1] In contrast to other antimicrotubule drugs like the vinca alkaloids, vincristine and vinblastine, that cause disassembly of cellular microtubules, paclitaxel promotes and stabilizes polymerization of the microtubules. This interferes with their normal function during mitosis, when they constitute the mitotic spindle, and in other vital cellular processes and can lead to cell death. By interfering with progression of the cells through mitosis, paclitaxel tends to arrest cells in the premitotic (G2) and mitotic (M) phases of the cell cycle when they are most sensitive to the effects of radiation and many cytotoxic agents.[2]

Paclitaxel has demonstrated activity in a wide range of human cancers. It was initially approved for the treatment of relapsed or refractory ovarian cancer. A recent study by the Gynecologic Oncology Group (GOG) demonstrated improved response rates and survival in patients with advanced ovarian cancer who were treated initially with a combination of paclitaxel and cisplatin, as compared to those treated with cisplatin and cyclophosphamide, which had been standard first-line treatment.[3] Paclitaxel is approved for the treatment of women with metastatic breast cancer. Response rates as high as 56–62% have been reported using paclitaxel alone.[4,5] It also has demonstrated significant activity as a single agent in cancers of the head and neck, small cell and non-small cell lung cancers, esophageal cancer, transitional cell cancer of the bladder, and germ cell tumors.[1]

The optimal schedule and dose of pactitaxel remain to be defined.[6] Initial clinical trials used a 24-hour infusion of the drug every 3–4 weeks, which required that treatment be administered in a hospital. Administration of the drug in the outpatient setting over three hours or even one hour became feasible by pretreating patients with steroids and antihistamines, which reduced hypersensitivity reactions. In a randomized study in relapsed ovarian cancer, the response rate to paclitaxel was not compromised by using a shorter infusion schedule but the relative efficacy of longer and shorter infusion schedules continues to be studied.[7] The shape of the dose-response curve for paclitaxel is not clear. Is there a threshold dose below which the response rate falls significantly? Is there a dose above which the response rate plateaus and further

ABBREVIATIONS USED

ABMT	Allogeneic bone marrow transplantation
APL	Acute promyelocytic leukemia
ATRA	All-trans form of retinoic acid
CHOP	Cyclophosphamide, doxorubicin, vincristine, prednisone
CML	Chronic myelogenous leukemia
COGRI	Clinical Oncology Group of Rhode Island
CPT-11	A camptothecin derivative
DIC	Disseminated intravascular coagulation
DNA	Deoxyribonucleic acid
G-CSF	Granulocyte colony stimulating factor
GOG	Gynecologic Oncology Group
GM-CSF	Granulocyte-macrophage colony stimulating factor
HIV	Human immunodeficiency virus
IFN-α	alpha Interferon
m-BACOD	Low-dose methotrexate with leucovorin rescue, bleomycin, doxorubicin, cyclophosphamide, vincristine, dexamethasone
MACOP-B	Methotrexate with leucovorin rescue, doxorubicin, cyclophosphamide, vincristine, prednisone, bleomycin
NHL	Non-Hodgkin's lymphoma
ProMACE-CytaBOM	Prednisone, doxorubicin, cyclophosphamide, etoposide, followed by cytarabine, bleomycin, vincristine, methotrexate with leucovorin rescue
RA	Retinoic acid (syndrome)
RAR	Retinoic acid receptor
SWOG	Southwest Oncology Group
WBC	White blood cell count

dose escalation buys only increased toxicity? Is the shape of the curve the same for all cancers? These are questions that are being addressed by clinical researchers at a number of institutions. Studies performed by the Clinical Oncology Group of Rhode Island (COGRI) have demonstrated that the dose-intensity of paclitaxel can be significantly increased by administering it weekly, instead of every three or four weeks, without causing excessive toxicity.[8] While results from this phase I study in non-small cell lung cancer are encouraging, it is too early to predict whether this schedule will prove to be superior to other ways of administering the drug.

Of even greater interest may be combinations of paclitaxel with other agents. Paclitaxel has demonstrated synergy with cisplatin and carboplatin in the laboratory. Clinical studies appear to confirm this activity. The efficacy of the combination of paclitaxel and cisplatin in ovarian cancer was mentioned above, and response rates as high as 60% have been reported for paclitaxel with either cisplatin or carboplatin in advanced non-small cell lung cancer.[9] In patients with advanced breast cancer, a response rate of 94% was recently reported for paclitaxel with doxorubicin (Adriamycin), but was accompanied by an alarmingly high rate of cardiotoxicity.[10] Studies of paclitaxel in combination with these and other cytotoxic agents are ongoing.

Paclitaxel appears to arrest cells at the phases in their cell cycle during which they are most sensitive to the effects of radiation. The COGRI has been studying the combination of weekly paclitaxel with radiotherapy, first in locally advanced non-small cell lung cancer and recurrent or unresectable primary brain tumors, and more recently in locally advanced cancers of the esophagus, stomach, and pancreas. Study of this effect is progressing from the local to the national level.

Major toxicities of paclitaxel include myelosuppression, particularly neutropenia that tends to be of a more rapid onset but briefer in duration than with most other chemotherapeutic agents, alopecia, and a cumulative peripheral sensory neuropathy that typically reverses when the drug is discontinued. With the shorter infusion schedules, mild to severe myalgias and arthralgias, the etiology of which is unknown, may develop 2–5 days after drug administration and can last for a week or longer. Nausea, mucositis or diarrhea are infrequent toxicities of paclitaxel alone, but can be significant when it is administered with other cytotoxic agents or radiation. In the phase I trials, disturbances of cardiac rhythm were reported, particularly bradycardias, but these rarely proved to be clinically significant; still it is recommended that paclitaxel be avoided in patients with significant atrioventricular or intraventricular conduction defects.[1]

> *Major advances in the treatment and prevention of neoplastic diseases may be imminent...However, the failure of well designed studies to confirm some "great treatment advances" cautions us to retain a healthy skepticism when evaluating promising, but preliminary results.*

At present, paclitaxel, alone or in combination, can be considered as first-line or second-line therapy for a variety of advanced cancers. While it seems likely that it will continue to play a major role in the foreseeable future, many questions about its optimal use remain.

Other New Agents

Docetaxel (Taxotere) is a taxoid like paclitaxel and has a similar mechanism of action. It has demonstrated activity in ovarian cancer, breast cancer, and non-small cell lung cancer.[11] Whether it has any advantages over pactitaxel, in terms of either its antitumor activity or toxicity profile, is unclear at this time.

Vinorelbine (Navelbine) is a semi-synthetic vinca alkaloid that appears to have more activity in common malignancies like breast cancer and non-small cell lung cancer and to cause less neurotoxicity than vincristine or vinblastine.[12] Suramin is a polysulphonated napthylurea that has demonstrated significant antitumor activity against hormone-refractory prostate cancer, but has a range of toxicities that may limit its usefulness.[13] Camptothecin derivatives, including topotecan and CPT-11, act by inhibiting topoisomerase-I, an enzyme critical to DNA replication.[14] Significant antitumor activity in the laboratory has been demonstrated and the derivatives are now undergoing clinical testing against a variety of cancers. Gemcitabine is a novel nucleoside analogue that both inhibits the production of deoxynucleotide triphosphates required for normal DNA synthesis and is incorporated into DNA as a false base, resulting in termination of DNA replication.[15] It is being studied in a number of cancers, including pancreatic cancer. Fludarabine (Fludara), 2-chlorodeoxyadenosine (Cladribine), and 2'-deoxycoformycin (pentostatin) are purine nucleoside analogues that interfere with the function of adenosine deaminase, leading to accumulation of deoxypurine nucleotides. Lymphocytes are particularly sensitive to the cytotoxic effects of these nucleotides; thus, these drugs are effective in the treatment of malignancies of B-lymphocytes, including chronic lymphocytic leukemia, hairy cell leukemia, and the low grade non-Hodgkin's lymphomas, but also can cause marked impairment of cell-mediated immunity, leaving patients susceptible to opportunistic infections.[16]

New Roles for Biologic Agents

Alfa-interferon in Chronic Myelogenous Leukemia (CML): Chronic phase CML may best be considered a premalignant condition that predisposes affected individuals to the inevitable development of a fatal malignancy, the accelerated and blastic phases of the disease. The presence of the Philadelphia (Ph) chromosome, a reciprocal translocation between the long arms of chromosomes 9 and 22 that creates the novel bcr-abl fusion gene, is a marker of the disease, though exactly what role it plays in the manifestations of the chronic phase of CML and its transformation to the accelerated or blastic phases is unknown.[17]

The duration of the chronic phase is variable and determines the patient's prognosis. In older series, the median survival of patients with CML was around three years. Prognostic models

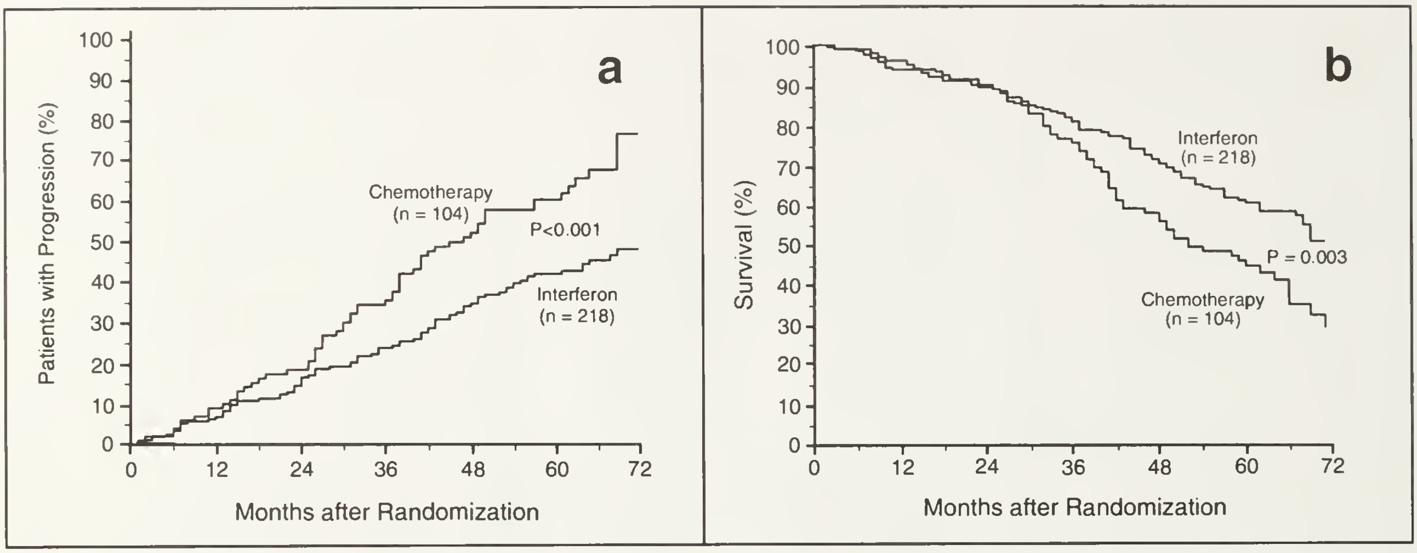

Figure 1. Disease progression to accelerated or blastic phase (a) and survival (**b**) of patients with CML treated with conventional chemotherapy (hydroxyurea or busulfan) or interferon alfa-2a. Reprinted with permission.[21]

have been developed that divide patients into good-, intermediate-, and poor-risk groups based on their characteristics at diagnosis. Comparing current results with older data can be confounded by changes in the distribution of patients between these subsets. While many CML patients still present with anemia, left upper quadrant pain, bone pain, and/or fever, sweats, and weight loss, more than 40% of patients are asymptomatic at diagnosis; the disease is picked up incidentally. While the proportion of patients in the three risk categories has shifted, the prognosis for patients who receive standard treatment has not changed.[18]

Conventional treatment for CML has changed little over the past 20–30 years. Busulfan, the first chemotherapeutic agent demonstrated superior to radiation therapy, was largely supplanted by hydroxyurea in the 1970s, due to its more predictable effects on blood counts and its lack of pulmonary and other organ toxicities. While both hydroxyurea and busulfan are usually effective at treating the symptoms and controlling the hematologic abnormalities of chronic phase CML, neither has been shown to significantly delay progression of the disease to accelerated or blastic phase or to suppress the clone of cells that express the Ph chromosome.

The only curative treatment for CML is allogeneic bone marrow transplantation (ABMT). In addition to the cytotoxic therapy that patients receive prior to the transplant, the donor marrow apparently exerts a graft-versus-leukemia effect that plays a major role in maintaining remission. ABMT is standard treatment for young (<40 years) CML patients who have a histocompatible sibling, and should be performed as soon after diagnosis as possible.[17] Unfortunately, only a small percentage of patients with CML have an appropriate donor, and while the age range for ABMT is being stretched, at some centers, up to 55-60 years, transplants in older patients or in patients with less than perfect matches have a higher mortality rate, primarily due to infections and complications of graft-versus-host disease.

That normal cells remain within the bone marrow, even when only Ph+ metaphases are found on cytogenetic analysis, is evidenced by the reappearance of Ph– cells after aggressive chemotherapy, although these cytogenetically normal cells typically disappear within a few months. Aggressive chemotherapy in chronic phase CML has not been shown to prolong survival and is not routinely used.[19] In addition, when bone marrow cells from patients with CML are cultured and grown in the laboratory, over time Ph– cells reappear, while the Ph+ cells dwindle in number. Thus, if an agent could be found that selectively inhibits Ph+ cells, normal hematopoiesis might resume, possibly delaying the progression of the disease to the accelerated and blastic phases.

The rationale for treating patients in the chronic phase of CML with alpha-interferon (IFN-α) came from observations that interferons demonstrate antiproliferative activity against normal and leukemic myeloid colony growth *in vitro* and that patients treated with interferons for other diseases often develop cytopenias. In the early 1980s, investigators reported the activity of daily injections of human leukocyte IFN-α in the treatment of chronic phase CML.[20] Subsequent studies demonstrated similar activity for recombinant IFN-α2b. Normalization of blood counts, referred to as a hematologic response, is seen in about 80% of patients treated with IFN-α, but in up to 70% of patients there also is evidence of selective suppression of the clone of abnormal cells, with the reappearance of Ph– metaphases. In about a third of the patients, less than 35% of metaphases remain Ph+; these patients are considered to have achieved a major cytogenetic response. Between 10–26% of patients will have a complete cytogenetic response, with no detectable Ph+ metaphases at some point during treatment.[18] Major cytogenetic responses are often durable with continued IFN-α treatment, and correlate with improved survival. More than 85% of these patients are alive at five years,compared to 70% of patients who achieve only a minor cytogenetic response and 30% of patients who fail to achieve a cytogenetic response. Analysis of available data suggests that IFN-α treatment improves survival for patients in all risk categories at diagnosis, but has the largest impact on patients in the good- and intermediate-risk categories, which now constitute almost 90% of patients at diagnosis.[18]

An Italian cooperative group randomized 322 newly-diagnosed patients with chronic phase CML to standard chemotherapy with hydroxyurea or busulfan or IFN-α.[21] The median time of progression to accelerated or blastic phase was significantly longer in the IFN-α group (>72 vs. 45 months), as was median survival (72 vs. 52 months) (Figures 1a and 1b). The progression and survival benefit was derived solely from the 30% of patients on the IFN-α arm who had significant cytogenetic responses, 90% of whom had evidence of a cytogenetic response by 14 months on IFN-α, though in many cases their best karyotypic response was not reached for two or more years.

IFN-α therapy does not cure patients with CML; even in patients with complete cytogenetic responses by karyotypic analysis molecular studies continue to demonstrate the presence of cells that contain the bcr-abl fusion gene. Side effects from IFN-α range from early flu-like symptoms, to which most patients become tolerant, to persistent fatigue, anorexia and weight loss, depression, insomnia, and sensory neuropathy, which result in dose reductions or discontinuation of treatment in 10–25% of patients. The optimal dose and schedule of IFN-α in chronic phase CML are unknown; at least one study suggests that much lower doses than the standard $5 \text{ X } 10^6$ U/m^2 SQ daily may be as effective with substantially less toxicity.[22] While these issues are being investigated, available data suggests that patients who are not candidates for ABMT should receive at least a 12 month trial of IFN-α and be monitored for any evidence of a cytogenetic response. In patients with any evidence of restoration of Ph– hematopoiesis, the IFN-α should be continued to see if they can achieve a major cytogenetic response, while non-responding patients can be switched to hydroxyurea and considered for less conventional therapies such as high risk ABMT, using marrow from a partially matched family member or a matched unrelated donor, high dose chemotherapy with autologous BMT or experimental agents.

IFN-α also may have a role as an antiproliferative agent in patients with multiple myeloma and low grade non-Hodgkin's lymphomas, particularly in patients with limited residual disease after chemotherapy, and in the treatment of Kaposi's sarcoma in HIV patients, malignant melanoma, and advanced renal cell cancer.

ATRA Therapy in Acute Promyelocytic Leukemia (APL): APL accounts for 5–15% of cases of acute myeloid leukemia (AML) in adults. It is characterized morphologically by an apparent maturation arrest at the promyelocyte stage of differentiation, with the bone marrow dominated by large, immature cells containing abundant azurophilic primary granules and easily identified Auer rods. Clinical features include a younger median age at presentation compared to other subtypes of AML, frequent presentation with leukopenia as opposed to leukocytosis, and a relatively favorable prognosis, with a 5-year disease-free survival rate of 35–45%. The prognosis, however, is tempered by a high mortality rate with standard induction chemotherapy. Between 10–20% of patients die early in the course of treatment from disseminated intravascular coagulation (DIC) that is triggered by the release of procoagulants from the abnormal promyelocytes with chemotherapy-induced cell lysis.

The characteristic cytogenetic abnormality of APL is a reciprocal translocation between the long arms of chromosomes 15 and 17, which can be identified in over 90% of patients with the typical clinical picture of the disease. This results in fusion of a gene called PML with a gene that encodes a nuclear receptor for retinoic acid, referred to as *RAR*-α.[23] Retinoids are vitamin A derivatives that play vital roles in embryogenesis and normal cell proliferation and differentiation. Of a number of retinoic acid receptors, the *RAR*-α receptor has a limited distribution, but is found in hematopoietic cells. The clinical application of retinoic acid in APL was stimulated by the discovery that it could induce differentiation in a human promyelocytic cell line in culture. It is postulated that the PML-*RAR*-α fusion somehow interferes with normal cellular differentiation signals mediated through the retinoic acid receptor, but that pharmacologic doses of retinoic acid may restore normal differentiation. The all-trans form of retinoic acid (ATRA) is used because of its affinity for cellular retinoic acid binding proteins.[24]

Studies performed in China demonstrated that a high percentage of APL patients could achieve remission with oral ATRA alone.[25] By inducing differentiation of the abnormal promyelocytes, the risk of inducing DIC essentially disappeared, and many patients achieved remission without going through marrow aplasia or severe cytopenias. Subsequent studies have confirmed this observation, but found that patients who did not receive consolidation chemotherapy often relapsed within a few months, whether or not ATRA was continued.[26] Thus, while ATRA induces differentiation of the abnormal promyelocytes, it does not eliminate the atypical clone of cells. In a European study of APL, 91% of patients treated with ATRA, with or without chemotherapy, achieved complete remission, compared to 81% with standard induction chemotherapy alone. All patients then received consolidation chemotherapy. At one year, 79% of patients who received ATRA were alive and free of disease, compared to 50% on the chemotherapy alone arm.[27] (Figure 2) It is likely that a high percentage of these remissions will be durable. Early analysis of a similar study performed in this country confirms the superiority of ATRA plus chemotherapy to chemotherapy alone. The most common toxicities of ATRA affect the skin and mucous membranes, including erythema, desquamation, paronychia, cheilitis, rhinitis, and dry mouth. Headache, bone pain, elevated liver enzymes, and hypertriglyceridemia are also common. Despite leukopenia at presentation, more than half of the patients with APL treated with ATRA will develop leukocytosis during treatment. A rising white blood cell (WBC) count may herald the development of the retinoic acid (RA) syndrome. This syndrome is characterized by fever, pulmonary interstitial infiltrates, pleural effusions, weight gain with peripheral and pulmonary edema due to capillary leak, and progressive respiratory distress. The cause of the RA syndrome is unknown, but signs and symptoms of it may appear in as many as a third of the patients treated with ATRA for APL. In one study, 9% of patients died of this complication of treatment, making it

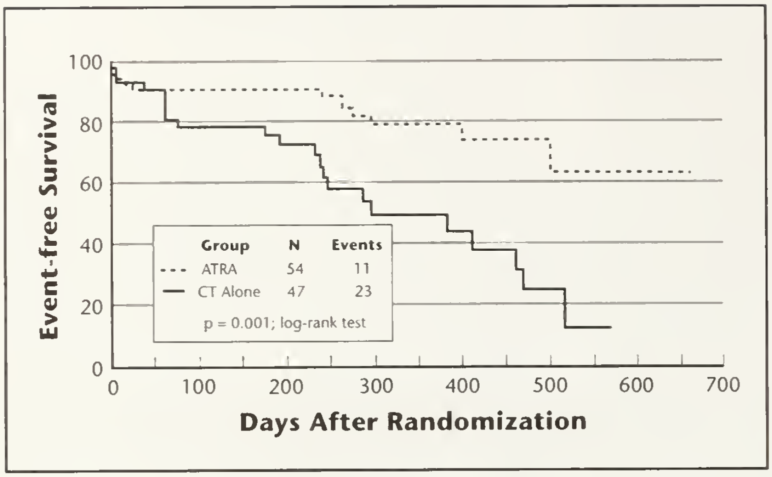

Figure 2. Kaplan-Meier estimate of event-free survival (event is defined as failure to achieve complete remission, relapse or death) in patients with APL treated with ATRA (with or without chemotherapy) or chemotherapy (CT) alone. Reprinted with permission.[27]

almost as frequent a cause of mortality as DIC is in patients treated with chemotherapy.[26] If the RA syndrome is suspected, the drug is stopped, steroids are administered, and the patient receives supportive care as indicated, including intubation if necessary. In the European study, induction chemotherapy was added to ATRA in patients who presented with an elevated WBC or who had a rapidly rising WBC during ATRA treatment; using this approach, no patients died or required intubation due to the RA syndrome, but many patients were given chemotherapy during induction therapy who would likely not have gone on to develop the RA syndrome.[27] The optimal timing of the addition of chemotherapy to ATRA remains to be determined.

The use of ATRA in APL is an example of using a biologic agent to induce differentiation of neoplastic cells, as opposed to using a cytotoxic agent. Retinoids also are being used to try to encourage normal differentiation of the oral and respiratory epithelium to prevent second cancers in smokers who have been treated for a head and neck or lung cancer. What role such agents may have in the prevention or management of other malignancies is unknown.

Other Biologic Agents

A variety of other biologic agents are currently in use or under development. The hematopoietic growth factors G-CSF, GM-CSF, and erythropoietin are used in patients with a variety of malignant and nonmalignant diseases. Thrombopoietin, which stimulates platelet precursors, is in initial clinical trials. Interleukin-2 has well documented activity in patients with malignant melanoma and advanced renal cell cancer and other interleukins are being studied for possible roles in the treatment of malignancies. Monoclonal antibodies, so-called magic bullets, are being used in conjunction with bone marrow transplantation in patients with lymphomas, and continue to be studied in patients with solid tumors.

New Concepts in Molecular Biology

Apoptosis, *bcl-2*, and *p53*: Apoptosis, also known as programmed cell death, is the body's way of maintaining balance between cell proliferation and cell death. In apoptosis, individual cells undergo nuclear pyknosis and systematic DNA fragmentation, increased cell density, and shrinkage; the cell membrane remains fairly intact until the cell is ingested by neighboring cells, minimizing the release of proteases and chemoattractant molecules that could induce an inflammatory response. In contrast, necrosis is characterized by clusters of cells exhibiting cellular swelling, degradation of organelles, and rupture of cellular membranes that release substances that elicit an inflammatory response. Apoptosis regulates the size of virtually all normal cell populations, but is especially prevalent in tissues with a high turnover rate. A number of genes that are highly conserved throughout evolution have recently been implicated as positive and negative regulators of apoptosis.[28]

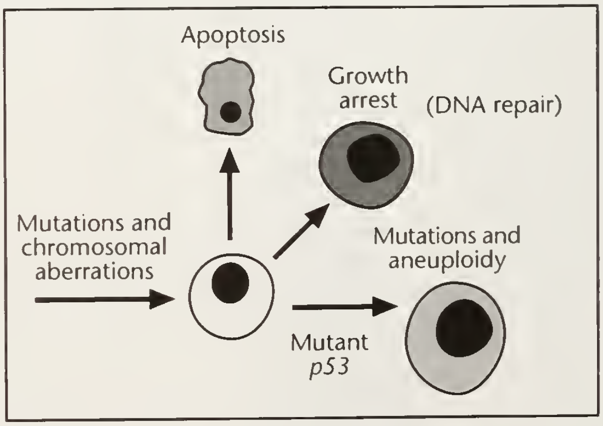

Figure 3. Control of cell proliferation, growth arrest and DNA repair, and apoptosis by normal *p53*. Reprinted with permission.[29]

In 1985 a gene called *bcl-2* was discovered at the site of the translocation between chromosomes 14 and 18 that is characteristic of the follicular B-cell non-Hodgkin's lymphomas. It was soon demonstrated that this gene promotes tumor formation not by stimulating cell proliferation but by blocking cell death. In humans the *bcl-2* gene is widely expressed in embryonic cells, but in healthy adults its expression is restricted to hematopoietic progenitor cells and other long-lived cells, including subsets of B- and T- lymphocytes. Overexpression of *bcl-2* has been reported in many hematologic malignancies as well as in a variety of solid tumors. The mechanism by which *bcl-2* protects cells from apoptosis is unknown, but it may protect cellular membranes from oxidative damage. If this is truly its mechanism of action, since oxidative damage is one of the major mechanisms by which many chemotherapeutic agents and radiation target malignant cells, cells that inappropriately express *bcl-2* may be less susceptible to anticancer therapy. Investigators have speculated that *bcl-2*, while not a classic oncogene, may enhance the oncogenicity of other deregulated genes by inhibiting apoptosis.[28]

The normal, or wild-type, *p53* gene appears to be an important component in the pathway that controls apoptosis. It is classified as a tumor suppressor gene, whose normal function is to prevent the growth of abnormal cells. By mechanisms that are still not completely understood, damage to DNA stimulates production of the *p53* nuclear protein, which in turn stimulates the production of other proteins that inhibit progression of the cell through DNA replication and mitosis, giving the cell a chance to repair the damage before the cell divides.[29] Conflicting growth regulatory signals during *p53* expression, sustained *p53* synthesis due to extensive DNA damage, or *p53* activation after irreversible commitment to replication can drive a cell to apoptosis (Figure 3). Downregulation or inactivation of *bcl-2* may be one of the mechanisms by which *p53* induces apoptosis. *p53* also appears to play an important role in senescence. Aging cells synthesize reduced amounts of *p53* inhibitors, which results in a reduction of the proportion of dividing cells in the population.

At least half of all malignant tumors have mutations or rearrangements of both copies of the *p53* gene, including 80% of colon cancers, 50% of lung cancers, and 40% of breast cancers.[29] These mutations result in either inadequate production of *p53* or the production of a defective version of the protein. The absence of functional *p53* allows cells to proliferate despite damage to DNA, which could result in the establishment of a malignant clone(Figure 4). In the Li-Fraumeni syndrome, affected individuals inherit mutations in the *p53* gene; they are at high risk of developing breast cancer, sarcomas, brain tumors, and other malignancies at an early age, presumably due to damage to or loss of their remaining normal *p53* allele (referred to as loss of heterozygosity).[30]

Cells deficient in normal *p53* are relatively resistant to chemotherapy- and radiotherapy-induced cell killing, at least in part by inhibition of apoptosis; cancer treatment thus may select for *p53*-deficient cells, which would then be resistant to subsequent treatment.[29] The important role played by *p53* in tumor development and proliferation may offer therapeutic opportunities, however, such as using gene therapy to insert an active copy of the *p53* gene into a *p53*-deficient cancer or the development of agents that activate the apoptotic pathway past the point at which *p53* acts.

Telomeres and Telomerase: At the ends of human chromosomes are telomeres, which are composed of multiple repeats of a simple nucleotide sequence. Telomeres appear to stabilize the ends of the chromosomes, protecting them from degradation and preventing loss of coding sequences from the 3' ends of the chromosomal strands during DNA replication; it is these expendable, noncoding sequences that are lost instead.[31] Telomere length correlates with the number of divisions cells can undergo in culture. Shortening of the telomeres may function as a type of mitotic clock in somatic cells; after so many divisions the telomeres are lost, so that subsequent divisions result in the loss of coding sequences and cell death.

Germ cells contain an enzyme called telomerase that prevents telomere shortening. Telomerase fills in the gap at the 3' end of the chromosomal strands left by normal DNA replication that would otherwise lead to shortening of the telomere, preventing succeeding generations from starting off with a shortened biological clock. Telomerase activity has been identified in malignant tissues from a number of sites, while the enzyme is absent from adjacent normal tissues and benign tumors; this appears to play a role in the immortalization of malignant cells.[31] In a current theory (Figure 5), increased telomerase activity is not responsible for malignancy. An initial mutation, such as the loss of the normal function of a tumor suppressor gene like *p53* results in increased cellular proliferation. Before the proliferating mutated cells reach a "crisis" caused by shortening of the telomeres, another mutation results in inappropriate expression of telomerase in a subpopulation of cells, which are then immortalized. Intriguing possibilities are raised by the prospect that many cancers may rely on the activity of telomerase. If this enzyme were inhibited, would the cancer cells become senescent and die? Beyond the field of cancer, the discovery of telomerase raises the possibility of manipulating the aging of cells, and perhaps the general loss of organ function that accompanies aging.

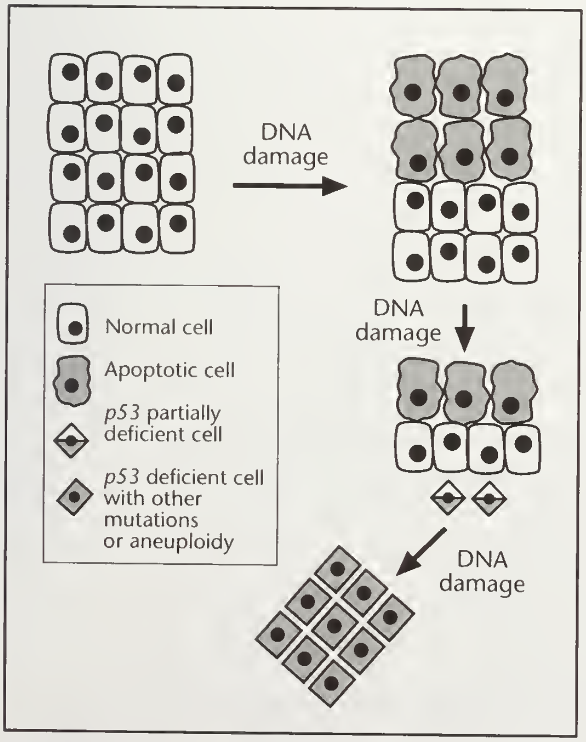
DNA damage
DNA damage
DNA damage
Normal cell
Apoptotic cell
p53 partially deficient cell
p53 deficient cell with other mutations or aneuploidy

Figure 4. Permissive effect of *p53* deficiency in the establishment of an abnormal clone. Reprinted with permission.[29]

INHERITED CANCER SYNDROMES

BRCA1 in inherited and sporadic cases of breast cancer: It is estimated that 5–10% of the cases of breast cancer in this country occur in women with an inherited predisposition to develop the disease. In 1990 a breast cancer susceptibility gene dubbed BRCA1 was mapped to the long arm of chromosome 17.[32] Mutations in this gene are believed to account for close to half of the cases of inherited early onset breast cancer and for most of the families with early onset breast and ovarian cancers. The gene encodes for a large protein. The structure of this protein is as yet unknown, but is believed to include two zinc finger domains, which are characteristic of DNA transcription factors.[33] Evidence suggests that BRCA1 may be a tumor suppressor gene, and that individuals who carry one defective copy of the gene are at risk of developing tumors if, by mutation or deletion, the

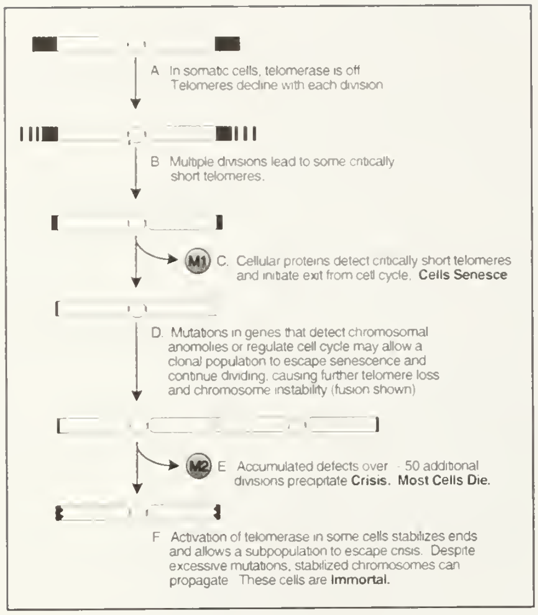
A In somatic cells, telomerase is off
Telomeres decline with each division
B Multiple divisions lead to some critically short telomeres.
M1
C. Cellular proteins detect critically short telomeres and initiate exit from cell cycle. Cells Senesce
D. Mutations in genes that detect chromosomal anomolies or regulate cell cycle may allow a clonal population to escape senescence and continue dividing, causing further telomere loss and chromosome instability (fusion shown)
M2
E Accumulated defects over ~50 additional divisions precipitate Crisis. Most Cells Die.
F Activation of telomerase in some cells stabilizes ends and allows a subpopulation to escape crisis. Despite excessive mutations, stabilized chromosomes can propagate These cells are Immortal.

Figure 5. Model for role of telomeres in cell senescence and telomerase in establishment of an immortal clone. Reprinted with permission.[31]

remaining active copy is lost or inactivated. Inherited mutations in BRCA1 appear to confer a lifetime risk of breast cancer that approaches 90%.[34] A number of sites of mutation of the gene have already been identified; however, the large size of the gene will make screening for mutations difficult unless a functional assay for the gene product can be developed.[35] Moreover, recommendations for assessing and counseling women with a family history of breast cancer are problematic; there are psychological, ethical, and legal implications of identifying at-risk individuals before we can prevent or even effectively screen for the malignancies to which they are prone. Suggested guidelines for primary care clinicians have been published.[36]

An important issue is the relevance of BRCA1 and other identified cancer family genes to the understanding of sporadic cases of breast and other cancers. Mutations in the BRCA1 gene have been identified in only 10% of sporadic breast and ovarian cancers. It has recently been reported, however, that while the BRCA1 gene product is located in the nucleus in normal breast tissue and in tumor cell lines not derived from breast or ovarian cancers, in cell lines derived from breast or ovarian cancers and in fresh cells from malignant effusions taken from patients with breast or ovarian cancer, the gene product was found in the cytoplasm, either exclusively or in addition to the nucleus.[37] The subcellular mislocation of the BRCA1 gene product in sporadic cases of breast and ovarian cancer suggests that abnormalities of the function of this gene may be fundamental to the development and/or progression of these cancers. The authors of the study suggest that the normal transport of the BRCA1 gene product to the nucleus may follow the same pathways used by steroid hormones and their receptors and that abnormalities in other molecules involved in that pathway may also be identified in inherited or sporadic cases of these cancers.

Other Inherited Cancer Syndromes: Other cancer family syndromes that have recently been described include the Li-Fraumeni syndrome (see above) and one linked to another inherited breast cancer gene referred to as BRCA2. A syndrome that is referred to as hereditary nonpolyposis colorectal cancer (to distinguish the affected families from those with familial polyposis syndromes) apparently arises as a result of a mutation in one of several genes that control repair of DNA mismatches.[38]

One Step Forward, One Step Back

CHOP versus more intensive regimens in intermediate grade NHL: The development of curative treatment for patients with advanced stage, intermediate grade non-Hodgkin's lymphomas (NHL), the most common of which is referred to as diffuse large cell or diffuse histiocytic lymphoma, has been one of the major successes of anticancer therapy over the past two decades. Of the so-called first generation regimens, CHOP(cyclophosphamide, doxorubicin, vincristine, and prednisone) became accepted as standard therapy, having demonstrated the ability to produce complete remissions in 45–55% of patients and apparent cures in 30–35%. In the 1980s, a variety of second and third generation regimens were piloted by major referral centers; new agents, including bleomycin, etoposide, and/or methotrexate with leucovorin rescue were added to CHOP, and the dose-intensity of treatment was increased. Complete remission and disease-free survival rates of 55–65% were reported with the newer regimens, but the patients treated on these nonrandomized studies were often

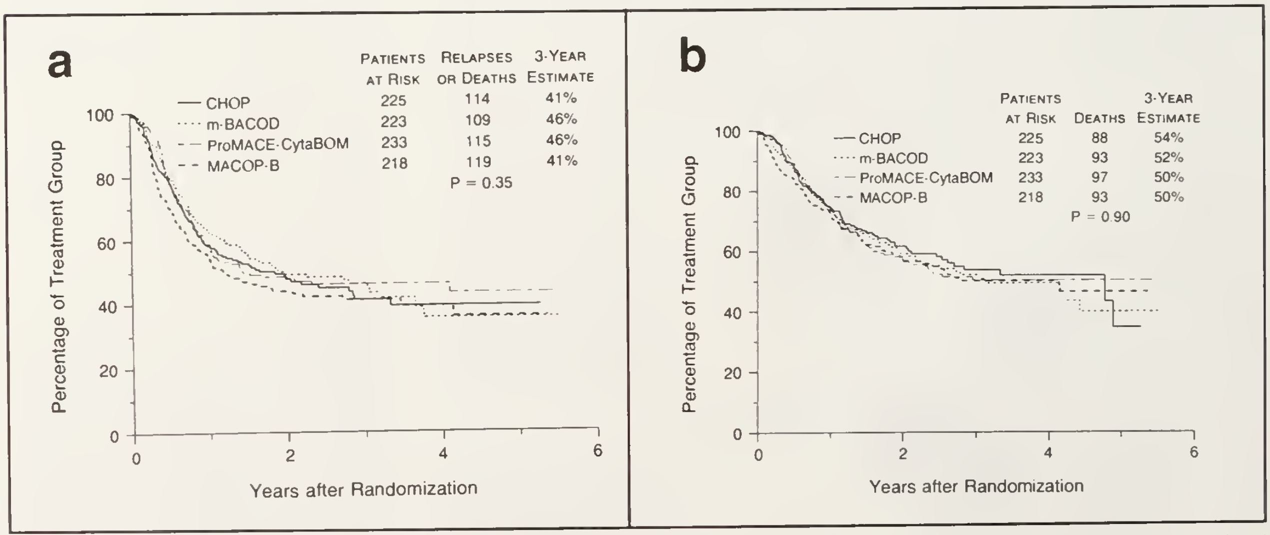

Figure 6. Relapse free (**a**) and overall (**b**) survival in patients with aggressive NHL treated with CHOP or one of three more intensive regimens. Reprinted with permission.[39]

younger and in better condition than the average patient with these lymphomas, and the newer regimens were associated with more toxicity and higher treatment costs than CHOP. In 1986 the Southwest Oncology Group (SWOG) initiated a randomized study comparing CHOP to three highly touted second and third generation regimens, m-BACOD, ProMACE-CytaBOM, and MACOP-B. The study included 899 eligible patients. The results were reported in 1993.[39]

While the more intensive regimens had slightly higher complete responses rates than CHOP (44% for CHOP vs. 48% for m-BACOD, 56% for ProMACE-CytaBOM, and 51% for MACOP-B), the differences were not statistically significant. The relapse-free and overall survival for all patients at three years were 44% and 52%, repectively, with no significant differences seen between the treatment arms (Figures 6a and 6b). Treatment-related mortality was only 1% with CHOP, while it was 3–6% with the other regimens; life-threatening and fatal toxicities were significantly more common with m-BACOD or MACOP-B than with CHOP or ProMACE- CytaBOM. There were no identified prognostic subgroups that significantly benefited from the more intensive regimens.

The results of this study suggest that CHOP should again be considered standard therapy for advanced stage, intermediate grade NHL. The study did not prove, however, that more intensive therapy is no better than CHOP, only that the drugs used in these regimens at the doses administered did not improve treatment results. More intensive therapy, with bone marrow or peripheral blood stem cell support, may be required to significantly increase complete response and disease-free survival rates or we may need to identify new, active drugs that can be added to or used in place of the drugs in the CHOP regimen to cure more of the 60–70% of patients who fail CHOP therapy. In any case, the results of the SWOG study should be viewed as a caution to anyone who would trumpet a major advance in cancer therapy based on pilot data and underscore the continued need for well designed, randomized studies before any treatment can become accepted as a new standard.

The next several years will likely witness the development of new therapies based on discoveries in one or more of the areas discussed above. We can hope that advances in these and other areas will allow us to make significant strides in the battle against cancer.

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Infectious Disease Challenges in the 1990's

Steven M. Opal, MD

These are challenging and rather troubling times for the discipline of clinical microbiology and infectious diseases in the United States. Despite a seemingly endless variety of new antimicrobial agents and vaccine candidates over the past several decades, it is rather sobering to note that infectious diseases and parasitic diseases continue to account for the greatest number of deaths of humankind worldwide. Interspersed with reports of remarkable successes (i.e. the eradication of polio from the western hemisphere, elimination of small pox, and the dramatic reduction in frequency of invasive Hemophilus influenzae infections by the use of the conjugate vaccine), there are disturbing reports of multidrug-resistant tuberculosis, highly resistant, nosocomially-acquired bacterial infections, and new outbreaks of highly lethal diseases such as the Hantavirus pulmonary syndrome, Ebola virus infection, and toxic Strep syndrome. Clinicians are beginning to lose some confrontations with multiple antibiotic-resistant bacterial pathogens, and researchers continue to be frustrated by our inability to bring the current AIDS epidemic under control.

This review will highlight some of the major infectious disease challenges that face clinicians in the United States today. While we should have every reason to be optimistic about our capacity to deal effectively with pathogenic microorganisms, it has become increasingly apparent that new treatment strategies will be complex, will require considerable effort, and will necessitate a long-term and concerted effort by clinicians, basic researchers, and patients alike.

ABBREVIATIONS USED

AIDS	Acquired immune deficiency syndrome
ARDS	Acute respiratory distress syndrome
AZT	Zidovudine
DIC	Disseminated intravascular coagulation
HGE	Human granulocytic ehrlichiosis
HIV	Human immunodeficiency virus
INH	Isoniazid
MDR-TB	Multi-drug resistant tuberculosis
PCR	Polymerase chain reaction
PZA	Pyrazinamide
RNA	Ribose nucleic acid

...focused education, judicious screening for HIV infection, reduction in frequency of multiple sex partners, and prevention of injection drug use are the most appropriate preventive strategies against the spread of HIV.

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THE VIRUS THAT WON'T GO AWAY

The statistics, while startling, fail to indicate the immense scope of the great human tragedy of the AIDS Epidemic and HIV infection. An illness that was considered a medical curiosity when first recognized in 1981 has become the leading cause of death among Americans between ages 25 and 44. As of April 1995, the Centers for Disease Control has recorded 282,220 deaths of Americans from AIDS since the beginning of the epidemic. The World Health Organization currently estimates that there are 4.5 million persons with AIDS worldwide.[1] This number may be as high as 12 to 14 million by the year 2000. While the rate of increase of new cases of AIDS in the United States appears to be slowing somewhat, there is no evidence that the epidemic is slowing in regions of Asia and Africa where explosive case rates have been reported.

Despite an exponential increase in the knowledge of this virus and the host response to it, current treatment strategies are limited and prospects for an effective vaccine in the near future are not good. Nonetheless, some new information about viral physiology and the dynamics of the cellular and humural immune response to HIV provide some insights that may prove useful in the management of this relentless and ultimately fatal disease.

Recent evidence indicates that HIV is replicating at exceedingly high rates within the human body.[2,3] It is estimated that up to 1 billion new virions are produced daily in an infected human being. The half-life of the virus in the systemic circulation is less than 48 hours. Continuous high-grade replication occurs throughout the lifetime of an infected individual, with maximum rates of replication occurring within the first few months of infection (prior to the development of a host immune response) and the last several months of life (where the immune response has been rendered ineffective). Up to 1 trillion virions are generated in the first few months of infection. Initially, the virus is genetically rather homogeneous but the high mutation rate of reverse transcriptase (approximately 1 mutation in every 1000 nucleotide replications) results in the rapid generation of a diverse array of genetic variants of HIV within a single person. These variants include virus particles with high replication rates and a tendency to generate syncytium formation. Point mutations along the reverse transcriptase gene of HIV result in variants that are no longer susceptible to reverse transcriptase inhibitors such as AZT.[4]

After an initial phase of uncontrolled replication, a vigorous cellular and humoral immune response develops against multiple antigenic components of the HIV particle. This leads to a deceptively stable phase of rather peaceful co-existence with the virus as the host remains asymptomatic. While this phase may persist for years or even decades, the virus gains the upper hand in this interaction with the host, which almost invariably leads to gradual destruction of the host immune response, resulting in opportunistic infections and full blown AIDS. Viral replication continues to occur while the host immune response struggles to contain the infection. A few "long term non-progressors"

Table 1
Examples of New Recognized Emerging Diseases

Disease	Organism	Geographic Range	Clinical Manifestations
Ehrlichiosis	*E. chaffeensis* or *E. phagocytophila*	Widespread (including RI) SE United States	Tick-borne summer illness, fever, headache, thrombocytopenia
Bacillary angiomatosis Cat-Scratch Disease	*Bartonella* (formerly *Rochalimaea*) *henselae*	Widespread	Vascular, lesions, ulcers, lymphadenopathy
Hantavirus pulmonary syndrome	hantavirus	SW United States and RI	ARDS, DIC
Ebola virus	filovirus	Kikwit, Zaire	Rapidly fatal, tropical hemorrhagic syndrome
Cyclospora spp.	protozoan	Nepal, Central America	Severe watery diarrhea
Cholera	*Vibrio cholerae* 0139	India, SE Asia	Completely new serotype, severe cholera

have been described, which are patients who remain asymptomatic with relatively normal CD4 cells in their systemic circulation for up to 12 years. These remarkable individuals appear to have a favorable cell-mediated immunity to multiple HIV antigens and also may be infected with less virulent strains of HIV. While these patients are exceedingly rare, they provide insight into the potential to control HIV infection in human populations. They also may provide the rationale for attempts at immune reconstitution and long-term management of HIV infected patients.

These new observations of the basic virology of HIV and the human immune response to the virus have many important implications in the management of HIV infection. First, it is important that we develop a more effective anti-viral strategy. The virus replicates at a very high rate and single agent therapy such as Zidovudine (AZT) alone only decreases the viral load by approximately 0.7 log.[4] More effective anti-retroviral agents, or preferably combinations of agents such as HIV-1 protease inhibitors or non-nucleoside reverse transcriptase inhibitors in combination with more traditional agents, result in lowering of plasma viremia by 2–3 log or more. Combination therapy appears to be the principal therapeutic strategy against HIV at present and for the near future.

Second, it is important to treat HIV at its onset before the immune system is irreparably damaged and while the virus is relatively homogeneous with smaller numbers of genetic variants (including resistant variants to anti-retroviral drugs). Treatment at the time of seroconversion or prior to infection (ie.prevention of perinatal transmission of HIV to infants born to HIV-infected mothers) are optimal times for anti-retroviral therapy.[5]

Third, immune-based therapy such as immune reconstitution and immunoadjuvants such as interleukin-2 may be useful but appear to be of maximal benefit if given simultaneously with combination anti-retroviral therapy. Immunotherapy might boost the already vigorous host immune response to the virus and further "tip the scales" in favor of the host in its interaction with HIV.

Fourth, vaccine strategies are undoubtedly going to be difficult and complicated. Multiple genetic variants of HIV exist and new variants are generated on a continuous basis. It is known that several major genetic subtypes (Clades) already exist in HIV. Clade B is the dominant strain of HIV in the U.S. while Clade E is the dominant strain in Asia. It is conceivable that these different genetic subgroups will require a polyvalent vaccine approach in order to prevent transmission of HIV to human populations. The problem of generating continuous high levels of mucosal immunity, dealing with multiple serotypes, and constant antigenic variation of this virus will be the greatest challenge to vaccine development in medical history.

Real progress has been made in the management of HIV-infected patients through the prevention and therapy of opportunistic infections. Prophylactic therapy for *Pneumocystis carinii*, toxoplasmosis, *Mycobacterium-avium intracellulare*, and secondary prophylaxis against Candida and Cryptococcal infections have now become standards of practice in the management for HIV-infected individuals. Prophylaxis against common pyogenic bacterial organisms is now routinely administered to children with symptomatic HIV infection. With the development of oral gancyclovir, it may be possible to provide prophylaxis against cytomegalovirus retinitis as well.

The HIV epidemic is undoubtedly the greatest challenge that faces infectious disease practitioners in the latter half of this century. Unfortunately, it does not appear that solutions to the AIDS epidemic will be forthcoming in the early phases of the 21st century. At present, it appears that focused education, judicious screening for HIV infection, behavior modification with reduction in frequency of multiple sex partners, and prevention of injection drug use are the most appropriate preventive strategies against the spread of HIV.

EMERGING PATHOGENS

Emerging pathogens are defined as microbial organisms, which have increased frequency in the last two decades or are anticipated to increase in the near future. Emerging pathogens come in two varieties: newly recognized infectious disease pathogens and established pathogens with new mechanisms of antimicrobial resistance (see Tables 1 and 2).

While a wide variety of emerging pathogens have been described throughout the U.S. and the rest of the world, many of these emerging pathogens have been recognized here in Rhode Island. These pathogens remind us that there is a need for continued vigilance in screening for new infectious agents, and that we do, indeed, live in a global community in which health problems anywhere in the world may have an effect on healthcare here in Rhode Island.

Ehrlichiosis: A newly recognized tick-transmitted rickettsial pathogen known as *Ehrlichia chaffeensis*, and a closely related species *Ehrlichia phagocytophila* have been found in southern New England. These are obligate intracellular bacterial pathogens similar to Rocky Mountain Spotted Fever (which also occurs in Rhode Island). Human monocytic ehrlichiosis (HME) is caused by *E. chaffeensis* and is particularly common in the summer months in the southeastern part of United States. The disease is primarily transmitted by the Lone Star tick (*Amblyomma americanum)*, but common ticks in our region, *Dermacentor variabilis* (the dog tick) and *Ixodes scapularis*, subspecies *dammini* (the deer tick) are now known to transmit the agent of human granulocytic ehrlichiosis (HGE), known as *E. phagocytophila*. Multiple vertebrate species carry Ehrlichia organisms but the exact nature of the non-human reservoir population for *E. chaffeensis* is not known.[6,7]

The disease is characterized by a summertime illness with associated fever, headache, myalgia, anorexia, arthralgia and general malaise. Approximately 20% of patients will have a macular skin eruption usually found in the lower extremities. The classic petechial lesions found in Rocky Mountain Spotted Fever are unusual with ehrlichiosis. Characteristic laboratory findings include thrombocytopenia, leukopenia, and elevations in liver-associated enzymes. The disease may be life threatening with gastrointestinal and CNS involvement. Immunocompromised patients, in particular AIDS patients, may be severely afflicted with Ehrlichiosis, which ultimately may be fatal. Diagnosis is usually made by specific serologic studies or by Polymerase chain reaction (PCR). Treatment is with tetracyclines that

Table 2
Antibiotic-resistant Emerging Pathogens
"Old Bugs with New Tricks"

Organism	Mechanism of Resistance	Clinical Manifestations
Multi-drug resistant tuberculosis	? Permeability block; other mechanisms	Progressive primary tuberculosis
Vancomycin-resistant enterococci	Altered target site	Nosocomial infections
Penicillin-resistant pneumococci	Low affinity penicillin-binding proteins	Pneumonia, meningitis
Penicillin-resistant meningococci	Low affinity penicillin-binding proteins	Meningitis
Third generation cephalosporin-resistant bacteria	Extended spectrum beta-lactamases	Nosocomial infection

need to be given in high dose for two weeks. Chloramphenicol does not appear to be effective. The quinolones and perhaps rifampin might be alternative treatments in patients who cannot tolerate tetracyclines. A vaccine against ehrlichiosis is under current development.[8]

***Bartonella (Rochalimaea)* Infections:** Evaluation of an obscure dermatologic condition in AIDS patients known as bacillary angiomatosis has led to the identification of a previously unrecognized pathogen known as *Bartonella (Rochalimaea) henselae*. This organism is a small, curved, fastidious, gram- negative bacillus that is difficult to isolate and culture and appears to be related to *Rickettsia* species and *Agrobacteria*. In AIDS patients, the organism produces a peculiar dermatologic condition with multiple vascular papules, which may ulcerate and may be confused with Kaposi's sarcoma. Pathologically, these lesions consist of vascular cells with epithelioid histiocytes and a fibromyxoid stroma that contain many pleomorphic gram-negative bacilli as demonstrated by special staining (Warthin-Starry). This discovery led to effective treatment with either erythromycin or doxycycline.

Subsequent to this discovery, it was found that previously recognized syndromes of uncertain etiology also were associated with infection with *Bartonella (Rochlimaea)* species.[9] These include peliosis hepatis (a vasoproliferative disease of the liver with multiple cystic blood-filled spaces in a fibromyxoid stroma) and Cat-Scratch disease. Further investigations revealed that the majority of patients with the common affliction of Cat-Scratch disease also had evidence of recent Rochlimaea infection. This organism is now known to be more closely related to Cat-Scratch disease than another causative organism, *Afipia felis*. Current evidence suggests that the most common cause of Cat-Scratch disease is *Bartonella (Rochalimaea)* species. Most domestic cats and 80–90% of patients with Cat-Scratch Disease have serologic evidence of infection with this organism.[10]

This is an important discovery in that it is now clear that there is an effective treatment for Cat-Scratch disease in the form of prolonged treatment with erythromycin, doxycycline or quinolones. Aminoglycosides are effective in disseminated infections, as is rifampin. Infection by this organism may be severe. Patients have been described with relapsing, febrile bacteremia, and, in some cases, endocarditis. The discovery of the *Rochalimaea* species has permitted the development of a clinically valid serologic test for Cat-Scratch disease and ended several decades of research into the etiology of this disease.

Hantavirus Pulmonary Syndrome: A cluster of cases of a rapidly fatal pulmonary syndrome in previously healthy young adults led to the recognition of a new disease known as Hantavirus pulmonary syndrome.[11] Hantaviruses are RNA viruses that are adapted to rodent species and belong to the virus family *Bunyaviridae*. These viruses are well-known throughout the world and are occasionally associated with human infection where they result in a viral hemorrhagic fever often with acute renal failure. Finding that Hantaviruses were endemic in the United States and could cause a fatal pulmonary syndrome was a great surprise and an important discovery.

This outbreak was first noted in 1993 in the four corners region in the southwestern United States. Sporadic cases now have been described throughout the U.S., including a recent fatal case in Rhode Island. The disease is transmitted to humans presumably through inhalation of rodent excreta. Illness is characterized by a rapid onset illness of fever, myalgias, headache, cough, and rapidly progressive acute respiratory failure. The disease is associated with a rapidly progressive ARDS-like (Acute respiratory distress syndrome) syndrome with histologic evidence of thin, hyaline membranes and absence of a significant inflammatory response in the lung tissue. Patients generally die of progressive pulmonary failure associated with hemoconcentration, lactic acidosis, thrombocytopenia, and evidence of Disseminated intravascular coagulation (DIC). The case fatality rate approaches 70%. Despite attempts to study antiviral agents and anti-inflammatory agents in this disease, no treatment has been shown to be effective other than supportive care. Surveys of rodent populations in southeastern New England have shown that the virus is endemic in common field mice in this part of the country. It is likely that sporadic cases of this pulmonary syndrome will continue to occur throughout the United States when rodent populations and virus levels are high and environmental conditions favor transmission to humans.[12]

Cyclospora Infections: A newly recognized parasitic cause of enteric infection and prolonged diarrhea has been described, belonging to a new species known as Cyclospora.[13] This disease was first recognized in Nepal but now has been found in Central and South America. It is becoming an increasingly frequent problem for international travelers returning to the United States. The organism is a sporozoan similar to *Cryptosporidium* species. It originally was described as a cyanobacterium or perhaps even a blue-green algae but has subsequently been shown to be a protozoan parasite. The organism has some interesting characteristics, including its ability to autofluoresce upon exposure to Ultraviolet light. This is useful in the diagnosis of cyclospora on stool examination. The organism causes a chronic, severe, watery diarrhea that may last several months. Recent evidence suggests that treatment with sulfa-trimethoprim may shorten the duration of illness and provide relief to many frustrated international travelers with chronic diarrhea.

Multidrug-Resistant Tuberculosis: The recent epidemic of multidrug-resistant (MDR) tuberculosis points out, all too clearly, the failure of our public health system to eradicate tuberculosis in the United States. Factors including homelessness, the HIV epidemic, migrant farm workers, recent immigrants with tuberculosis, and lack of public health priority to ensure adequate treatment and follow-up have led to a resurgence of tuberculosis, particularly in the inner cities of New York, Florida, and southern California. MDR strains of tuberculosis now are found sporadically throughout the country and represent a significant threat to the public health that requires immediate attention.[14]

Fortunately, recent efforts to control this epidemic have been successful in reducing the incidence of tuberculosis over the past two years. This has been accomplished by refocusing our efforts to manage tuberculosis effectively through aggressive contact tracing, improved infection control measures, and the widespread acceptance of directly observed therapy in the treatment of patients infected with tuberculosis.[15] The spread of multidrug resistant strains of tuberculosis within the hospital setting led to numerous outbreaks among hospitalized patients and health care workers alike. This has prompted the Occupational Safety and Health Administration to promulgate a new series of regulations relating to infection control procedures for patients with tuberculosis. Improvements in hospital engineering with improved air-handling systems, use of ultraviolet light, and strict adherence to respiratory isolation have been remarkably successful in reducing the number of secondary cases of tuberculosis within the hospital setting. The most controversial aspect of this control program has been the institution of submicron filtered, personal respirators for health care workers involved in the care of tuberculosis patients. While the wisdom of these infection control measures continues to be questioned, health care workers generally have learned to accept the use of these masks and other precautions.[16]

It is clear that multiple drug resistance to standard anti-tuberculosis chemotherapy is problematic because we do not have sufficient alternative treatments for these patients. Work on the development of new anti-tuberculosis drugs and a long overdue vaccine against tuberculosis has now become a major research priority.

The first step toward understanding of drug resistance in tuberculosis has been the recent discovery of the mechanism of Isoniazid (INH) resistance. Resistance is due to the loss of a gene (known as *KatG*) which encodes for a mycobacterial catalase enzyme. The loss of this bacterial enzyme interferes with the mycobactericidal effect of INH on the bacterium. If the gene is re-introduced into resistant organisms through transfection, the organism becomes susceptible to INH again. This is an important discovery that has stimulated a great deal of interest in other mechanisms of drug resistance in mycobacterial species, and will likely lead to new treatment strategies in the control of tuberculosis.[17]

Current recommendations for tuberculosis include an initial two-month treatment strategy using four drugs (INH, rifampin, PZA and ethambutol or streptomycin). Directly observed therapy is now the standard of care in the management of tuberculosis. Following the two month induction therapy, an intermittent treatment strategy is followed, with two or three times weekly anti-tuberculous drugs based on the susceptibility patterns of the tuberculosis isolate. Patients with MDR strains may be treated with alternative agents such as quinolones, amikacin, ethionamide or carbapenems. It is vitallly important that physicians caring for patients with active tuberculosis notify the state health department. This assures that appropriate contact tracing is performed and that secondary cases are prevented. Rhode Island has largely been spared from this epidemic of MDR tuberculosis. Our good fortune may continue through continued vigilance and appropriate care of tuberculosis patients.[18]

Vancomycin-Resistant Enterococci: Vancomycin has been the principal backup drug to treat methicillin-resistant *Staphylococcus aureus*, *Clostridium difficile*, coagulase-negative Staphylococcal infections, penicillin-resistant pneumococci, and high-level, ampicillin and aminoglycoside-resistant strains of enterococci. Resistance to this glycopeptide antibiotic was unheard of until the late 1980's when transferrable antibiotic resistance to vancomycin was first discovered in enterococcal species in France.[19, 20, 21] Unfortunately, this resistance determinant now has spread throughout the world and has become increasingly problematic in the United States. We have had several nosocomial epidemics of vancomycin-resistant enterococci in Rhode Island hospitals, which is likely to continue to be problematic in the foreseeable future.[22] Resistance is due to plasmid-mediated or transposon-mediated mutated enzymes that alter the intracellular target site for vancomycin-binding and its antimicrobial action. Vancomycin usually binds to the terminal D-alanine-D-alanine moiety of the cell wall precursors for bacteria. The resistance genes mediate an enzyme that changes the substrate specificity such that instead of generating a D-ala-D-ala peptide, a depsipeptide is synthesized. D-lactate or D-betahydroxybutrate is substituted for D-alanine. This alteration does not allow vancomycin to bind to precursors of peptidoglycan synthesis and disrupts its antimicrobial activity.

Vancomycin-resistant enterococci represente a major threat to our standard therapy to nosocomial infections in that these enterococcal species frequently express high level ampicillin-and aminoglycoside-resistance. Treatment options are limited to agents such as chloramphenicol, high dose erythromycin (if an enterococcal urinary tract infection is present), Teichoplanin (vanB) tiecoplanin (if the VanB phenotype is present), or experimental agents such a pristinomycin (synercid).

Strict contact isolation is necessary when managing the patient with a vancomycin-resistant enterococcal infection. The organism may contaminate the surface of the patient as well as sheets, bedding, medical instruments, etc. Evidence suggests that the organism is spread primarily through fomites and the hands of health care workers in the hospital setting.[23]

Penicillin-Resistant Pneumococci: Low level (0.2 to 2.0 mcg/ml) and high level (>2 mcg/ml) resistance to penicillin is now in pneumococcal isolates throughout the United States.[24] These organisms have been widespread for several years in southern and eastern Europe and have spread to the United States. Resistance is caused by altered penicillin-binding proteins that have low affinity for penicillin, yet continue to function in cell wall synthesis. Penicillin-resistant strains of *Streptococcus pneumoniae* are more common in children than adults. This is probably related to the frequent exposure of children to antibiotics in the treatment of pharyngitis and otitis media. Unfortunately, penicillin-resistant strains of *Streptococcus pneumoniae* also are more likely to be resistant to other commonly employed antibiotics such as the macrolides (erythromycin), tetracyclines, sulfa-trimethoprim and cephalosporins.[25]

The principal therapeutic strategies includes vancomycin or high dose, third-generation cephalosporins. These penicillin-resistant strains of pneumococci point out the importance of preserving the therapeutic efficacy of vancomycin. If vancomycin-resistance were to develop in pneumococci, we would be in serious trouble indeed. The presence of penicillin-resistant *Streptococcus pneumoniae* also points out the urgent need to develop a more effective vaccine strategy against the pneumococcus. It is anticipated that the conjugate vaccine under development may allow for a more effective vaccine approach to pneumococcal infections in the future.

Numerous challenges remain in our continuing struggle to control microbial pathogens of humankind. Much basic research and clinical investigation remains before we can claim victory over infectious diseases or even before we can live in peaceful coexistence with the microorganisms of the world. Dedicated and innovative researchers are needed in the field of infectious diseases to meet the challenges posed by these most resourceful and fascinating organisms.

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Recent Advances in Pulmonary Medicine

Michael A. Passero, MD

> *"Where there is much desire to learn, there of necessity will be much arguing, much writing, many opinions; for opinion in good men is but knowledge in the making."*
>
> Milton, *Areopagitica*

The published abstracts of the 1995 International Conference of the American Thoracic Society contained over 5000 presentations, demonstrating an irrepressible thirst for new knowledge and research! The National Cystic Fibrosis Meeting had over 2500 participants. Obviously, one person cannot assimilate and analyze this great body of new knowledge in pulmonary medicine. In my review of recent advances, I tried to pick some relevant and useful topics, but the reader is cautioned that the choices were limited by my own experiences and bias. I suspect another author, given the same task, may have chosen an entirely different group of advances.

CYSTIC FIBROSIS

Although our understanding of the genetic cause of cystic fibrosis continues to evolve, a recent breakthrough in managing cystic fibrosis is the recognition and treatment of the inflammatory component. The role of *Pseudomonas* infection in exacerbating the lung disease is well recognized. Also, there has been increasing evidence that damage to the lung results from the host inflammatory response, especially the production of interleukin 8 and the influx of neutrophils into the airways. Some direct approaches to reduce the host inflammatory response in cystic fibrosis lung disease have included glucocorticoids, non-steroidal anti-inflammatory agents, pentoxifylline, fish oil, and antitrypsin. Alternate-day, low-dose (1mg/kg) prednisone has been tried, but its use is limited by side effects.[1] High dose ibuprofen (20–30mg/kg BID) slowed the progression of cystic fibrosis lung disease over a four-year period.[2] The annual rate of decline of FEV_1 was 88% slower for ibuprofen-treated patients in the 5–13 year age group. Side effects were minimal. Cystic fibrosis patients age 5–13 years who have an FEV of 60% predicted or better should be evaluated for high dose ibuprofen. Ibuprofen levels must be followed for effective therapy.

ABBREVIATIONS USED

BID	Twice daily (*bis in die*)
BIPAP	A respirator technique that provides both positive pressure inspiratory support and positive expiratory pressure via a tight-fitting face mask support and end expiratory pressure
COPD	Chronic obstructive pulmonary disease
FEV_1	Forced expired volume in 1 second
GI	Gastro-intestinal tract
HIV	Human immunodeficiency virus
IL	Interleukin
INH	Isoniazid
NO_2	Nitrogen dioxide
TB	Tuberculosis

Much progress in cystic fibrosis gene therapy has occurred. Since 1993, more than 70 individuals have received gene therapy delivered by modified adenoviruses. Researchers have demonstrated the introduction of the gene into humans who have cystic fibrosis and have achieved gene expression in both nasal epithelium and airways.[3] Other vectors are being considered, such as liposomes as a method to deliver gene therapy to the target airway. Some additional recent approaches to cystic fibrosis therapy include: the use of dornase alfa, an aerosolized recombinant human deoxyribonuclease, and aerosolized amiloride and uridine triphosphate, which is still experimental, to correct ion transport defects and, perhaps, clearance of mucus.[4]

ASTHMA

Anti-inflammatory agents such as cromolyn sodium, nedocromil sodium, and glucocorticoids now are recommended as essential to maintenance therapy of moderate to severe asthma. These agents are directed against the airway inflammation thought to play a significant role in asthma pathogenesis; presumably, chronic anti-inflammatory use will diminish the chronic airway thickening and damage found in long term-asthma. Although the anti-inflammatory agents are gaining wide acceptance, many are asking, "do β-agonists make asthma worse?" Several studies claim that β-agonists may actually worsen the frequency of asthma and increase asthma mortality.[5,6] The intensity of this debate has been heightened by the release of long acting β-agonists such as salmeterol. Recently, however, Ziment and McFadden reanalyzed and refuted most of this data, pointing out methodological flaws.[7,8]

It is not clear whether increased β-agonist use is the cause or the result of severe asthma. McFadden comments "...there is no convincing evidence that these drugs unfavorably modulate the responsiveness of the tracheobronchial tree in patients with asthma or reduce the protection from constrictor stimuli in a clinically meaningful way." In summary, although we should be using anti-inflammatory agents in our moderate to severe asthmatic patients, β-agonists are safe in recommended doses and are a reliable treatment for the symptoms of acute asthma.

Why do corticosteroids fail to control some asthmatics? Recently, a spectrum of glucocorticoid receptor-binding abnormalities were reported in peripheral blood monocytes from chronic asthmatics. These binding abnormalities were more pronounced in patients with poorly controlled asthma and associated with elevated serum levels of eosinophil cationic protein and soluble 1L-2 receptor. In addition, the diminished glucocorticoid receptor binding activity is thought to be an acquired defect mediated by cytokines (interleukins 2 and 4).

Spahn et al recently studied 12 asthmatic patients who were poorly controlled, despite high dose aerosol inhaled corticosteroids and an average of 20mg of prednisone daily.[9] The glucocorticoid receptor binding abnormalities found in these patients were reversed by a burst of high dose glucocorticoids (30mg of prednisone BID x

7–10 days) and there was an associated reduction in eosinophil cationic protein levels. The authors indicated that the decreased glucocorticoid-receptor binding affinity found in poorly controlled asthma is reversible and may be driven by inflammatory mediators. These findings may lead to a pulse steroid approach to chronic asthma in the future.

PULMONARY EMBOLISM

Why do hypoxemia and hypocapnia occur after pulmonary embolism? Santolicandro et al studied 10 patients at the time of diagnosis and 10-14 days after heparin treatment, including evaluation of right heart catheterization data, and assessment of ventilation-perfusion ratio distribution and angiography.[10] Hypoxemia was caused by both ventilation-perfusion abnormalities and reduced mixed venous O_2. Diffusion limitation and intrapulmonary shunt did not contribute to the hypoxemia. There was a broad spectrum of ventilation-perfusion abnormalities in these patients suggesting that different mechanisms prevail in different patients. Recovery from hypoxemia was also variable; it could persist for months. In the recovery period, ventilation usually normalized before perfusion, but not always. Hypocapnia was a result of hyperventilation. These findings help explain the variability in clinical presentation seen in patients with pulmonary embolism.

WEANING

Widespread dissatisfaction with traditional weaning parameters (blood gases, minute ventilation, respiratory rate, and respiratory force) has led investigators to try new criteria. Weaning may fail because of an imbalance of respiratory muscle capacity and respiratory demand. Muscle weakness, fatigue or a high respiratory demand result in rapid shallow breathing. A "shallow breathing index", the ratio of respiratory rate to tidal volume in liters, has been proposed for the assessment of weaning:[11]

$$\text{“Shallow breathing index”} = \frac{\text{respiratory rate}}{\text{tidal volume}} = f/VT$$

The measurement is made during one minute of spontaneous breathing through an endotracheal tube. Yang and Tobin demonstrated that if the shallow breathing index was greater than 105 ($f/VT > 105$), there was a high negative predictive value for weaning (0.95).[11] If f/VT was < 100, there was a high positive predictive value for weaning success (0.78). The lack of a close to 100% predictive value, however, has delayed acceptance of this criteria. Recently, Epstein evaluated patients who met the criteria for weaning success, (that is $f/VT < 105$) but failed weaning.[12] He found that 13 of the 14 patients failed because of congestive heart failure, upper airway obstruction, aspiration, encephalopathy or a new pulmonary process. Thus, the false positive rate of 0.22 can be explained by processes for which the f/VT is physiologically unlikely to predict success or failure.

Much progress in cystic fibrosis has occurred. Since 1993, more than 70 individuals have received gene therapy delivered by modified adenoviruses.

✻

In summary, about 80% of patients with an $f/VT < 105$ can be extubated unless the above processes are present. Measuring the "shallow breathing index," f/VT, is a simple and effective measurement for predicting weaning and should be used by physicians managing respirator patients.

The importance of optimizing the weaning time is underscored by Torres et al.[13] They studied 40 patients who were weaned but needed re-intubation. These patients were compared with matched controls for ventilation dependence times. Forty-seven percent of the patients who were re-intubated developed nosocomial pneumonia compared with 10 % of controls. Torres et al concluded that re-intubation is a risk factor for ventilator-associated pneumonias.

RESPIRATORY MUSCLES

Respiratory muscle strength has been of major interest because of advances in pharmacology, respirator management and lung reduction surgery. Gallagher reviewed the data demonstrating that high dose steroids cause significant respiratory muscle weakness in patients with auto-immune disease.[14] This also probably occurs in other patients similarly treated. Gallagher cautioned clinicians that respiratory myopathy must be considered as a cause of deterioration in patients with lung disease on moderate to high dose steroids.

Does aminophylline strengthen the diaphragm? New data seem to indicate a beneficial effect. Wanke et al demonstrated a positive effect of aminophylline on diaphragmatic contractility of the exhausted diaphragm at different lung volumes.[15] Gauthier et al showed that aminophylline potentiates contractility to a greater extent at short fiber lengths under both fresh and fatigued conditions.[16] The authors cautioned that their results need further study to assure their clinical relevance.

SLEEP APNEA

Sleep apnea, characterized by repeated apneic events, arterial hypoxemia, and sleep disruption, is thought to be part of a spectrum of sleep-related breathing disorders. These range from snoring, the mildest disorder, to hypoventilation and apnea in sleep with marked daytime somnolence and cardio-respiratory failure. Bearpark et al used home monitoring to evaluate snoring and sleep apnea in 294 men aged 40–65 years.[17] Eighty-one percent snored more than 10% of the night and 22% for more than half the night. Twenty- six percent were found to have sleep apnea. There was a relatively low correlation between percent of night spent snoring and sleep apnea. Obesity seemed related both to snoring and sleep apnea. The authors concluded that in middle-aged men, snoring and sleep apnea are common and they are associated with obesity.

Recent reviews of auto accident data indicate a higher rate of accidents in sleep apnea patients. The American Thoracic Society Committee on Respiratory Neurobiology and Sleep issued a statement providing guidance for physicians who treat sleep apnea patients who drive.[18] The recommendations included educational programs to increase public and professional awareness of disordered sleep and the recognition of sleepiness. The high-risk driver is a person with severe daytime sleepiness and history of a motor vehicle accident. Such patients should be educated and warned about driving risks associated with sleepiness. Patients with sleep apnea should be promptly diagnosed and treated, and reassessed within two months. Physicians must make themselves aware of state laws regarding reporting of high-risk drivers. There is insufficient evidence to suggest this level of caution for drivers with lesser forms of sleeplessness, for any given level of apnea, or for persons without a history of motor vehicle accidents. Physicians who deal with sleep apnea patients should review the committee's recommendations in their entirety.

THE HEPATOPULMONARY SYNDROME

Lang and Stoller reviewed the data base on the hepatopulmonary syndrome.[19]

It is defined as the triad of liver disease, increased alveolar-arterial gradient, while breathing room air, and evidence of intrapulmonary vascular dilatations. Patients present with the signs and symptoms of liver disease, including GI bleeding, esophageal varices, ascites, palmar erythema, and splenomegaly. Dyspnea is common and digital clubbing, cyanosis, dyspnea, platypnea (dyspnea induced by the upright position) and orthodeoxia (arterial deoxygenation worsening in the upright position) may occur. There is a correlation between spider nevi, pulmonary vasodilatation and gas exchange abnormalities.

Other important features are chest x-ray abnormalities, especially increased basilar interstitial and pulmonary vascular markings. The presence of the intrapulmonary vascular dilatations can be confirmed using contrast enhanced echocardiography using indocyanine green, perfusion lung scanning, and pulmonary arteriography. The patients with the most severe hypoxemia have diffuse pulmonary vascular dilatation that produces increased shunt and ventilation-perfusion mismatch. The responses to almitrine bismesylate, somatostatin, and indomethacin have been disappointing. Although the mechanism of the hepatopulmonary syndrome is unknown, reversibility after liver transplant suggests that liver transplant may be indicated for some patients. The authors raise many questions about diagnosis and management in their discussion of future prospects.

TUBERCULOSIS

One third of the world's population has been infected with *Myobacterium tuberculosis*. McKenna et al studied the effect of immigration on the epidemiology of tuberculosis in the US.[20] They found that the proportion of persons with TB who were foreign-born rose from 21.6% in 1986 to 29.6% in 1993. During that eight- year period, most foreign-born persons with TB were from Latin America or Southeast Asia. Fifty-five percent of immigrants with active tuberculosis were diagnosed within their first five years in the US. The authors argue for better worldwide control of the disease and improved control in the US. Cantwell et al reviewed the distribution and sources of increased tuberculosis in the US for 1985 to 1992.[21] They found that increases in the number of cases were concentrated in racial/ethnic minorities, persons 25 to 44 years of age, males, and foreign-born. Foreign-born cases accounted for 60% of the total increase. HIV had the greatest impact on morbidity. The authors called for more effective screening of immigrants and HIV infected patients. Bloch et al surveyed drug resistant TB in the US.[22] *They found resistance to one or more antituberculosis drugs in 14.2% of cases*. Resistance to isoniazid or rifampin was 9.5% in cases found in 35 counties in 13 states. New York City contributed 61% of the nation's multi-drug resistant cases. The relative risk of multi-drug resistant TB in New York City was non-Hispanic Blacks > Asian Pacific Islanders > Hispanic > non-Hispanic whites. The authors pointed out that 10% of the nation's TB patients are resistant to isoniazid and/or rifampin, and therefore greater use of four drug regimens and directly observed therapy is necessary.

How does the situation in Rhode Island compare with national figures? Table 1 shows the data for 1993 and 1994. The overall drug resistance rate is high in Rhode Island and resistance patterns show significant resistance to at least one drug. The relatively high number of drug resistance cases implies we must apply Bloch et al's conclusion to Rhode Island patients: Four drug therapy and directly observed therapy are indicated, with aggressive, optimal patient management to ensure completion of therapy.

AIR POLLUTION

Pulmonary effects of air pollution continue to be of great concern. Recent work has focused on the effects of individual pollutants. Ozone has been shown to produce cough, reduce exercise performance, increase airway reactivity, and cause reversible reductions in FEV_1. Whether asthmatics are more sensitive to ozone remains controversial. Weymer et al studied whether ozone worsened or produced exercise-induced asthma in known asthmatics.[23] Although all subjects had a reduction in FEV_1 at the highest ozone exposure levels (0.40 parts per million), ozone exposure for one hour did not worsen exercise-induced asthma. Hazucka et al noted that, in the United States, there is an early morning peak in nitrogen dioxide (NO_2) because of exhaust emissions from morning rush hour traffic.[24] This is followed by an ozone peak about four-six hours later, resulting from the sun's ultraviolet light acting on the NO_2. Accordingly, the effect of sequential exposure to NO_2 followed by ozone was studied in healthy women. Although nitrogen dioxide did not reduce

Table 1
Resistance to Anti-Tuberculosis Drug in RI

	1993	1994
No. of TB cases in RI	64	56
No. of drug-resistant cases	10	7
Overall drug resistance*	25.6%	16.7%
Resistance patterns:**		
Resistant to 1 drug	12.8%	9.5%
Resistant to at least INH and Rifampin	5.1%	2.4%
Resistant to other 2+ drug combinations	7.7%	4.8%

* Denominator is No. of isolates tested for drug sensitivity.
** Breakdown of overall drug resistance.
Source: Courtesy of L. Nacar, RI Department of Health

FEV_1, it significantly worsened ozone-induced reductions in flow. These findings suggest that nitrogen dioxide exposure can "sensitize" the airways to ozone, and result in airflow reductions greater than those resulting from ozone exposure alone.

Schwartz studied the effects of airborne particles and ozone on hospital admissions in the elderly in Detroit, Michigan.[25] An increase in either airborne particles or ozone concentration was associated with an increased number of admissions for pneumonia and COPD, but not asthma. Similar results have been reported from Birmingham, Ontario and New York. Current air quality standards are not strict enough to protect some patients from increased morbidity from these pollutants.

New studies also emphasize the need to control smoking as a source of indoor air pollution. Wang et al studied the association between parental cigarette smoking and children's pulmonary function.[26] Nine million American children under age five live with at least one smoker. This study showed that in school age children, a decrement in pulmonary function is associated with maternal smoking. This appeared to be a combination of a persistent deficit related to earlier, perhaps *in utero*, exposure and a further reduction related to current smoke exposure. These results suggest that efforts to reduce maternal smoking will enhance the pulmonary health of our children.

NEW TREATMENTS FOR COPD

Since late 1993, lung reduction surgery has become a popular treatment for patients with emphysema.[27] Unfortunately, there is little literature on variations and outcomes of this procedure. The procedure clearly has value as a "bridge" to lung transplantation for some patients have lived almost two years following the procedure.[28] Yet controlled studies about longer term results are lacking.

Although heart-lung and double lung transplants have been performed for advanced chronic obstructive pulmonary disease (COPD), single lung transplants have become more common. The advantages of single lung transplant are: 1) it is technically easier, 2) one donor serves two patients, and 3) there is potential for re-transplantation in the event of failure. Mal et al reported on 20 patients with chronic obstructive pulmonary disease who received a single-lung transplant.[29] Although lung function remained stable in some patients, others experienced a decline secondary to bronchiolitis obliterans. Four required retransplantation. The authors commented that, although single lung transplant does not return pulmonary function to normal, patients can still lead a normal life. All forms of lung transplantation are troubled by a high incidence of decline in lung function as the follow-up period lengthens.

Noninvasive positive pressure ventilation, administered with a tight-fitting nasal mask and a BIPAP type of respirator, may reduce the need for intubation for patients with acute respiratory failure, especially those with chronic obstructive pulmonary disease. In a study in Providence, RI, Kramer et al showed that the need for intubation was reduced from 73% in the control group to 31% in patients treated with noninvasive positive pressure ventilation.[30] Patients who had respiratory arrest, hypotension, uncontrolled arrythmias, upper airway obstruction, inability to control secretions, and inability to cooperate were excluded from the study. Heart rate, respiratory rate, dyspnea scores, and maximal inspiratory pressures were all improved in the treated group. Duration and cost of hospitalization, however, were not affected. Noninvasive positive pressure ventilation may be an additional option for selected patients with COPD and respiratory failure.

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Update in Nephrology

Michael J. Maher, MD, and Lance D. Dworkin, MD

This review will focus on newer treatment strategies of which the primary care physician should be aware and will focus on number of recent studies that have provided important insights into the management of patients with hypertension, acute and chronic renal failure, and diabetes mellitus.

INTERVENTIONS IN ACUTE RENAL FAILURE

Despite advances in renal replacement therapy, acute renal failure (ARF) results in a 50% mortality. Although a variety of interventions have been proposed to attenuate the course of ARF and reduce mortality, few new therapies have been shown to be definitely beneficial. A review by Conjer examined the results of several recent clinical trials.[1] The use of diuretics and vasoactive substances and new forms of dialytic therapy were examined.

There is little evidence that either mannitol or loop diuretics have any effect on the course of acute renal failure, except, perhaps, in the post-transplant patient. Several studies have documented that furosemide has no effect either on the rate of decline in renal function or on overall mortality. Some studies have suggested that loop diuretics, early in the course of ARF, may increase urine flow and that this may accelerate the rate of recovery of renal function;[2] however, these studies were uncontrolled and it is possible that the response to diuretics may have reflected less severe renal failure rather than an actual amelioration of the illness.

ABBREVIATIONS USED

ACE	Angiotensin converting enzyme
ANP	Atrial natiuretic peptide
ARF	Acute renal failure
AT	Angiotensin
CHF	Congestive Heart Failure
ESRD	End stage renal disease
GFR	Glomerular filtration rate
MAP	Mean arterial pressure
MI	Myocardial infarction

The debate regarding the utility of vasoactive peptides such as dopamine and atrial natiuretic peptide (ANP) remains active. Theoretically, in addition to causing a naturesis, these substances can increase renal blood flow and, thereby, attenuate the course of ARF, particularly when it is the result of an ischemic event. Results of the trials performed so far have been mixed, with no study showing that either ANP or dopamine reduces mortality or the need for dialytic therapy.Certain dialysis membranes have been shown to activate complement and, therefore, may have deleterious effects on recovery of renal function in acute renal failure. Recently, biocompatible dialysis membranes that have less of a propensity to activate complement have come into clinical use. Hakim et al compared the outcome of ARF in patients receiving dialytic therapy with biocompatible membranes to those dialyzed with bioincompatible membranes.[3] Their findings suggest that the newer compatible membranes can shorten the course of nonoliguric ARF and reduce mortality. At this time, it is recommended that all nonoliguric patients with acute renal failure be dialyzed with biocompatible membranes. This recommendation does not apply to those patients with oliguric ARF or those on chronic hemodialysis.

PROPHYLAXIS IN CONTRAST INDUCED NEPHROPATHY

Radiocontrast induced tubular damage is a common cause of acute renal failure. Patients who are at high risk for developing contrast nephropathy are those with diabetes or underlying renal disease. Despite the frequency with which it occurs, the exact mechanism of renal injury following contrast administration is not fully understood. Internists are frequently asked to prescribe prophylactic measures for patients prior to administration of a dye load. Various regimens have been proposed including the use of mannitol, furosemide, intravenous fluids, or calcium channel blockers. Few clinical studies have been performed to evaluate these regimens, and firm recommendations have been elusive.

Solomon et al reported the results of a large clinical trial, comparing the administration of mannitol or furosemide plus normal saline to administration of one half normal saline alone in 78 patients with chronic renal insufficiency undergoing cardiac catheterization.[4] They found that the group receiving fluids alone had a lower incidence of ARF than those receiving normal saline plus diuretic. Based on the results of this study, they recommended administration of 1/2 normal saline, 1cc per kg per body weight per hour over the 12 hours prior to, and following catheterization, without concomitant diuretics in patients with renal insufficiency undergoing catheterization. Whether or not the small increases in serum creatinine observed in this study had any effect on length of hospital stay or overall morbidity is unclear. To date, there are no definitive studies that support the use of calcium channel blockers as prophylaxis against contrast-induced ARF.

MANAGEMENT OF DIABETIC NEPHROPATHY

Diabetic nephropathy is marked by progressive proteinuria, azotemia and eventual development of end stage renal disease (ESRD). It has long been felt that once diabetic nephropathy is present, progression to ESRD is inevitable. In fact, diabetes is currently the leading cause of ESRD in the United States accounting for one-third of all dialysis patients. Uncontrolled studies suggested that treatment of hypertension slowed the rate of decline in kidney function in diabetic patients.

The captopril study has now documented that ACE inhibitors are superior to other drugs in preventing renal failure in patients with diabetic nephropathy. This was a randomized, controlled trial in which patients with type 1 diabetes and nephropathy were given captopril or placebo.[5] The authors observed in the captopril group a 50% reduction in the number of patients experiencing a doubling of serum creatinine over a three year period. Secondary endpoints such as death or the need for renal replacement therapy (dialysis or transplantation) were also significantly lower in the captopril group. In a subsequent report examining the same data base, Herbert et al described outcomes in the subset of diabetic patients with nephrotic range proteinuria.[6] This subanalysis revealed that 7 of 42 patients receiving captopril had remission of their nephrotic syndrome, whereas only 1 of 66 patients receiving placebo remitted. In those patients who did not have a complete remission of the nephrotic syndrome, those receiving captopril still had a significantly greater reduction in their 24-hour urinary protein excretion than did the control group.

All patients in the captopril study had type I diabetes and it is not possible to draw definitive conclusions regarding the use of ACE inhibitors in patients with type II diabetes from these data. Nevertheless, most clinicians feel that the etiology of nephropathy in type II diabetics is similar to that in type I, and that ACE inhibitors should be given to this group as well.

The Diabetic Control and Complication Trial Research Group examined the effects of intensive insulin therapy on the progression of diabetic nephropathy in type I diabetics.[7] This trial compared the effects of standard glycemic control versus intensive insulin therapy on microvascular disease including diabetic nephropathy. Intensive insulin therapy reduced the incidence of microalbuminuria by 39%, and that of macroalbuminuria by 54%. Of note, patients in the intensive insulin therapy group suffered a significant increase in symptomatic hypoglycemic episodes.

On the basis of the above studies, the National Institute of Diabetes and Digestive and Kidney Diseases has recommended that all patients with diabetic nephropathy be treated with an ACE inhibitor. In cases in which an ACE inhibitor is not well tolerated due to hyperkalemia or worsening of renal function, administration of a low dose should still be attempted and other, additional medications used to control hypertension. Attempts should also be made to achieve tight glycemic control.

Annual screening for microalbuminuria (albumin excretion rate of 30–300mg/24hrs) should be performed in all patients with type I diabetes who are over 12 years of age. Screening for microalbuminuria should also be done in all patients with type II diabetes who are under the age of 70. Although the 24 hour urine collection is more accurate, screening with a spot albumin to creatinine ratio is also adequate. If the ratio is less than 30 mg albumin/gram of creatinine, the study can be repeated in one year. If the ratio is between 30-300 mg/gm, the test should be repeated within three months. If it remains in this range, the patient should be considered to have early diabetic nephropathy. If it is greater than 300 mg/gm, the patient is likely to have clinical diabetic nephropathy and should be treated as such. Patients with microalbuminuria or overt nephropathy should be started on an ACE inhibitor even in the absence of hypertension, and the dose should be titrated up as tolerated. The albumin to creatinine ratio can then be monitored to assess efficacy of therapy.[8]

It has long been felt that once diabetic nephropathy is present, progression to ESRD is inevitable. In fact, diabetes is currently the leading cause of ESRD in the US, accounting for one-third of all dialysis patients.

Protein Restriction and Progression of Renal Disease

Protein restriction was first used to delay the onset of symptoms in patients with renal failure by reducing the production of uremic toxins. Animal and human studies also suggest that protein restriction actually slows the rate of decline of renal function in patients with chronic renal insufficiency. The Modification of Diet in Renal Disease Study Group examined the effects of dietary protein restriction and antihypertensive medication on the rate of decline in renal function in patients with renal insufficiency of various etiologies.[9] This study examined 585 patients with moderate renal insufficiency (GFR 25–55 cc/min) and assigned them to either a regular or a low protein diet (1.3 vs 0.8 g/kg/d), and to usual or lower than usual blood pressure control (MAP108 vs 92 mmHg). Two hundred fifty-five patients with more severe renal dysfunction (GFR <25 cc/min) also were studied and assigned to similar blood pressure control groups and to either a low or a very low protein diet with amino acid supplements.

In the first group with moderate renal disease, patients maintained on the low protein diet or with a lower blood pressure showed an initial more rapid rate of decline of their renal function, which was attenuated in the later months of the study. In patients with more pronounced renal dysfunction, there was a slower rate of decline in patients who were able to comply with the very low protein diet. In both arms of the study, patients with baseline protein excretion of greater than 3 gm/24 showed a slower rate of decline when their blood pressures were maintained at lower than usual levels. Unfortunately, the magnitude of the effect of protein restriction to slow the rate of decline in the patients on the lower protein diets was marginal, and it is not clear whether this would have been sustained. In addition, there was a very real risk of malnutrition in these patients that may counterbalance the possible positive effects.

Current recommendations are that patients with heavy proteinuria and hypertension should be maintained at blood pressures lower than previously recommended (MAP <92). Additionally, patients with moderate renal insufficiency may benefit from a diet that supplies 0.8 g/kg of protein per day, and that patients with severe renal insufficiency can be prescribed a very low protein diet. If these interventions are to be undertaken, however, it is critical that the diet is high in non-protein calories, and that nutritional status be monitored closely. Therefore, although potentially beneficial, the nutritional risks of such therapies, and difficulties in compliance and dietary counseling, make the prescription of such a diet impractical for most patients.

Calcium Channel Blockers and Risk of Myocardial Infarction

Recent attention in the lay as well as medical literature has focused on the potential risks of calcium channel blockers as antihypertensive therapy. A correlation has been observed between the use of short-acting calcium channel blockers and an increased risk of myocardial infarction (MI). Psaty et al published the results of a case control study that compared 623 hypertensive patients who were free of documented coronary artery or vascular disease but had an MI between 1986–1993, with 2032 control hypertensive patients who had not.[10] After controlling for age, race, and other risk factors for coronary artery disease, the authors found a statistically significant increase in the relative risk for myocardial infarction in those patients receiving calcium channel blockers. Additionally, this risk appeared to be greater in those on higher doses of these medications.

Similarly, Furberg et al published the results of a meta-analysis of trials of calcium antagonists and reached the same conclusion.[11] While the results of these studies are disconcerting, there are several problems with the data that make application of the findings to clinical practice premature. The editorial accompanying the study by Psaty reminds us of the difficulties in interpreting data from either a meta-analysis or case control study.[12] Given that clinicians often prescribe various forms of antihypertensive therapy for specific reasons, it is impossible to adequately control for all the factors that could potentially affect the endpoint of myocardial infarction.[12] In addition, these studies evaluated the effect of older, short-acting calcium channel blockers on the risk of MI. These short-acting agents cause reflex stimulation of the sympathetic nervous system that may increase cardiovascular risk, however, these changes are not seen with the newer, long-acting preparations. The findings of these studies underscore the need for randomized prospective studies to further evaluate this issue. The current recommendation of the Joint National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure is that diuretics and beta blockers be used as first line agents for the treatment of essential hypertension. Calcium blockers and ACE inhibitors are also acceptable agents for many patients and patients currently receiving calcium antagonists need not have their antihypertensive regimen altered.

Angiotensin II Receptor Antagonists

Recently, a new class of antihypertensive agents has become available, the angiotensin receptor antagonists. These agents work by specifically blocking angiotensin II receptors, that mediate the vasoconstrictive actions of angiotensin II, stimulate the sympathetic nervous system and release aldosterone. Unlike ACE inhibitors, these agents do not inhibit angiotensin converting enzyme (also known as kininase). Because they inhibit kinin degradation, ACE inhibitors cause bradykinin levels to increase leading to cough and, rarely, to angioneurotic edema. Clinical studies to date have shown the A II receptor antagonists to have a more favorable side effect profile and no increase in cough or angioedema has been observed.[13] Several studies suggest, on the other hand, that A II blockers are about as effective as ACE inhibitors in controlling blood pressure. At this time, the effects of A II antagonists on the renal hemodynamics and proteinuria in diabetic patients are not well delineated, however, studies are underway to examine this question. Therefore it cannot be assumed that these agents will have the same effect on the course of diabetic nephropathy as do the ACE inhibitors. Though little impact on serum creatinine has been reported, these agents also should be used with caution in patients with severe CHF, known renal artery stenosis, or renal insufficiency from other causes.

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Public Health Briefings

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Judith Feldman, MD, MPH, and John P. Fulton, PhD

Poor Ascertainment of Violence Against Women Hampers Surveillance

Wendy Verhoek-Oftedahl, PhD, Joann Lindenmayer, DVM, MPH, and Beatriz Perez, MPH

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While violence against women is a leading cause of injuries to women, injuries represent only the tip of the iceberg of violence levied against women. According to a recent study of domestic violence published in the Journal of the American Medical Association, victims of violence who present with injuries represent less than 25% of acute cases of domestic violence.[1] (Acute cases are those in which domestic violence is considered to be the underlying cause of the complaint for which medical care is sought.) Upwards of 20% of acute cases may present with respiratory problems, notably bronchitis or upper respiratory infections. Other conditions symptomatic of violence against women include chronic pain, stress, anxiety, depression, recurrent genitourinary infections, and complaints without physiologic explanations.[2,3] Of all women presenting as the result of acute domestic violence, little more than 10 percent will be identified without active screening.[1]

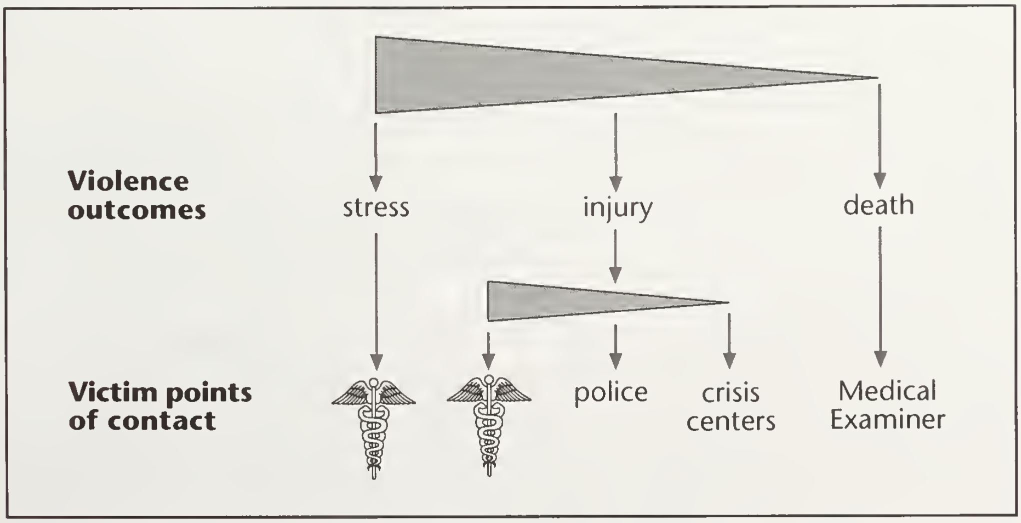

Figure 1. Surveillance of violence against women: role of health care providers.

The Injury Prevention Program of the Rhode Island Department of Health (the Department) received a grant from the Centers for Disease Control and Prevention to improve surveillance and identification of abused women, and to improve the coordination of victim services. Under this grant, data sources for tracking violence against women in the state (Table 1) were evaluated and found to be sorely lacking. Using available data, it is not even possible to calculate such basic statistics as incidence and prevalence rates.

PROBLEMS WITH EXISTING SOURCES

1. Problems with Definitions

To establish a surveillance system, we need to define what we want to track. The terms violence against women, domestic violence, and family violence tend to be used somewhat interchangeably. While the populations described by each term overlap, the definitions are not mutually inclusive. The terms child abuse and elder abuse further complicate the issue. Moreover, the types of abuse are often referred to as physical, sexual, and emotional, and include threats and intimidation. Attempts to define the populations at risk are often based on age, gender, and victim-offender relationship classifications. Which of these terms best describes a 16-year-old badly beaten by her husband, a 52-year-old woman injured by her father, or a young woman raped on a first date? What about violence occurring in gay or lesbian relationships, or threats or perceived threats? Ultimately, attempts to define and classify violence result in subgroups of the population falling through the cracks. In order to quantify the problem in Rhode Island, we need to collect data on the whole spectrum of violence and not be hampered by our own definitions. We can then vary the sensitivity and specificity of our surveillance system better to determine the burden of violence against women in Rhode Island and coordinate services for maximum benefit.

Data sources are grossly inadequate for assessing the incidence and prevalence of domestic violence in the state.[1] To make matters worse, existing data collection systems in RI only permit identification of women whose injuries require hospitalization. Police domestic violence reporting forms (DV-1's), legally required for all incidents of domestic violence, are not being used consistently. Court data are incomplete because they are only partially computerized. Perpetrators with charges not specific to domestic violence, but which involve domestic violence, such as stalking, cannot be distinguished from other cases in court records.

2. Lack of Practical Mechanisms to Quantify Cases

If active screening is instituted in health care settings, mechanisms to flag incident cases of violence against women need to be developed. Without such mechanisms, surveillance of violence would require time- and resource-intensive medical record reviews on an ongoing basis. If a diagnostic code such as the ICD-9 injury code 995.81, "adult maltreatment syndrome NEC" (includes battered spouse, battered woman), was routinely used, incidents of violence against women could be readily selected from hospital discharge, trauma registry, and emergency department databases. Ideally, the code used to flag incident cases would be one that could be used in conjunction with the standard ICD-9 diagnostic codes for both injury and noninjury (e.g. stress-related) cases. Consideration also should be given to identification of women who are chronically abused but whose current complaint may not be attributable to abuse.

3. Data Sources Skewed in Legal System

Currently, medical databases ascertain only victims with injuries requiring hospitalization or those serendipitously identified. The police data (DV-'1s) identify only those cases where the victims seek police help, and cases where family members, friends, or neighbors intervene and contact legal authorities. The RI court database (RIJSS) ascertains only those cases arraigned with domestic-specific charges. The result is a skewed picture and an inability to quantify violence against women in RI.

PHYSICIANS' ROLE IN SURVEILLANCE CRITICAL

Across the country, programs addressing violence against women are involving health care providers in the identification and surveillance of violence. As can be seen in Figure 1, health care providers are the first points of contact for the largest number of women in a continuum of violence that often begins with emotional abuse manifesting as stress and stress-related illnesses, and later culminates in physical injuries and, in extreme instances, death. Over the continuum of violence, women classically present more and more frequently for treatment of physical and emotional problems.

1. Active Screening

Active screening by physicians will enable the identification of many more victims of abuse than are identified through conventional means. This, in turn, will enable us to improve assessment of the burden of violence in the state.

2. Appropriate Patient Education and Referral

Early identification provides the opportunity for early intervention, before the violence escalates to serious or fatal injuries. Physician involvement lets women know that violence is unacceptable and unnecessary. Appropriate referral of women to support services ensures that women have timely access to the help they need.

3. Documentation

Careful documentation is critical, not only to facilitate provision of services to women, but to afford them access to the legal safeguards developed to protect them.

4. Physician Involvement at the Policy Level

Active support of the development and implementation of institutional procedures and protocols for screening, safety evaluation, documentation of abuse, and referral for appropriate services is critical for successful screening and management of violence against women. Institutional support for providers is essential to empower them to take an active role in identifying violence and referring victims for help. Institutional support for victims is essential to guide them through the sometimes tortuous process of breaking the cycle of violence.

In a recent survey, Emergency Department health care providers in RI cited lack of training, lack of workable institutional protocols, and lack of 24-hour support services as major barriers to the identification and treatment of violence against women.[4] The Department's Violence Against Women Prevention Program, recognizing the need for provider training and on-site advocacy programs, has obtained funding from the Centers for Disease Control to facilitate the development of comprehensive training and advocacy programs. During 1996, programs developed with community agencies and health care providers will be piloted and should greatly enhance ascertainment and treatment of violence against women.

EVERYONE WINS

If health care providers become more involved in the surveillance process, everyone wins.

1. Broken Cycle

The first step in breaking the cycle of violence is recognition of the problem. Early identification saves untold suffering of victims, families, and friends. Not only is the recovery period shortened, but whole families may be salvaged.

2. Improved Safety of Women

The immediate benefit will be an increase in the safety of women and a decrease in the number of injuries. An important added benefit will be an in

For information

On screening for domestic violence call:

- Meghan McGrath, Hospital Advocacy Program for Abused Women, Rhode Island Rape Crisis Center, (401)421–4100

On victim services call:

- The Rhode Island Coalition Against Domestic Violence Hotline, (800)494–8100
- The Rhode Island Rape Crisis Center, (401) 421–4100

Table 1
Data Sources for Surveillance of Violence Against Women

Emergency Department
- RI Hospital Emergency Medicine Group Billing Database
- Rhode Island Hospital Emergency Department Survey

Acute Care Hospitals
- Rhode Island Hospital Trauma Registry
- Rhode Island Hospital Clinical Social Work
- Women and Infants Hospital

Primary Care Providers
- Harvard Community Health Plan of New England
- Providence Ambulatory Health Care Foundation

Mental Health
- Butler Hospital
- The Providence Center

Rhode Island Department of Health
- Family Health Comprehensive Prenatal Services Program Database
- Forensic Laboratory
- Hospital Discharge Database
- Injury Program Sample of Injury-Related Emergency Department Visits
- Medical Examiner
- Rhode Island Health Interview Survey
- Vital Records Death Certificates

Victim Advocacy Services
- Rhode Island Coalition Against Domestic Violence
- Rhode Island Rape Crisis Center

Law Enforcement
- Police Domestic Violence Reporting Forms (DV-1's)

Justice System
- Office of the Attorney General: RIJSS Prosecution Database
- Temporary Restraining Order Offices

Note: Represents data sources evaluated to date. Additional data sources are currently under review.

crease in the safety of children living with these women.

3. Heightened Public Awareness and Decreased Societal Acceptance

As screening for violence becomes routine, the public will understand that while a man's home may be his castle, abusive or violent behavior is not acceptable in any setting.

4. Avoidance of Unnecessary and Potentially Harmful Medical Interventions

Accurate diagnosis of medical complaints will avoid unnecessary and potentially harmful tests, procedures, and treatments for psychogenic illnesses.

5. Decreased Individual and Societal Costs

Early identification and intervention in the continuum of violence will not only result in decreased pain and suffering but can also result in substantially decreased costs of medical, legal, and rehabilitative services.

6. More Accurate Assessment of the Burden of Violence

A united effort by health care providers, the Department, providers of victim services, and law enforcement agencies to address the public health problem of violence against women will result in more accurate assessment of the burden of violence against women in the State. This, in turn, will give us the capability to monitor trends, and to plan and to evaluate the effectiveness of interventions.

Violence against women is a real public health problem that cannot be effectively addressed without collaboration among physicians, other health care providers, the Department, and community victim service, social service, and law enforcement agencies. Physicians represent the major point of contact for women who are victims of violence, and physicians, by virtue of their profession, are trusted healers. The physician's role in surveillance of violence against women is critical.

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Health by Numbers

Rhode Island Department of Health
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Edited by Jay S. Buechner, PhD, and William J. Waters, Jr., PhD

Mortality from Chronic Obstructive Pulmonary Disease

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The group of lung diseases that are labeled "chronic obstructive pulmonary disease and allied conditions" (COPD) were the fourth leading cause of death in Rhode Island and in the United States in 1994, after diseases of the heart, malignant neoplasms, and cerebrovascular diseases. The conditions comprising COPD are characterized by chronic airway obstruction or slowing of forced expiratory flow, and include chronic bronchitis, emphysema, and asthma, as well as other, less well defined, lung diseases. Of the 9,468 decedents in Rhode Island in 1994, 393 (4.0 percent) were determined to have died from COPD. The large majority (311 or 79 percent) of COPD deaths were attributed to the underlying cause "Chronic airway obstruction, not elsewhere classified," one of the diseases included in the residual category "Other COPD" used with mortality statistics. (Figure 1)

It is estimated that as much as 82 percent of COPD mortality is attributable to cigarette smoking.[1] However, despite a general decline in smoking rates in Rhode Island and nationally in recent years, the mortality rates from COPD have been increasing over time in both populations, an effect attributed to the long latency between smoking onset and death from COPD.[2] In fact, the COPD mortality rates for the past three years in Rhode Island and the United States are the highest recorded in recent history. (Figure 2)

Mortality rates for COPD in Rhode Island have exceeded those for the United States in most years, as is true for many smoking-related diseases. Over the five years from 1990 through 1994, the state's rate averaged 2.9 percent higher than the national mortality rate, exceeding the national rate in three of those years. (Figure 2) This excess represents a decline from the previous decade, during which Rhode Island's rate exceeded the national rate in all ten years, by an average of 12.9 percent. Over the period from 1980 through 1994, the COPD mortality rate for Rhode Island rose by 30.2 percent, much slower than the increase of 54.7 percent in the national rate.

Death from COPD is almost totally confined to persons of late middle age or older. In Rhode Island, 97 percent of all COPD deaths occur among persons ages 55 or older, and 88 percent occur among persons ages 65 and older. Mortality rates increase rapidly with age even within this age range, peaking among those ages 85 and older. (Figure 3) Due in great part to their smoking histories, males ages 55 and older are more likely than females of the same ages to die from COPD. The level of excess mortality among males relative to their female counterparts increases with age from an excess of 22 percent among persons ages 55 through 64 to an excess of 150 percent among persons ages 85 and older.

As the effects of reduced smoking rates are seen, COPD mortality rates in Rhode Island and the United States will peak and begin to decline. The closing of the gap between state and national rates seen during the first half of this decade may be the first indication of this expected reversal in Rhode Island.

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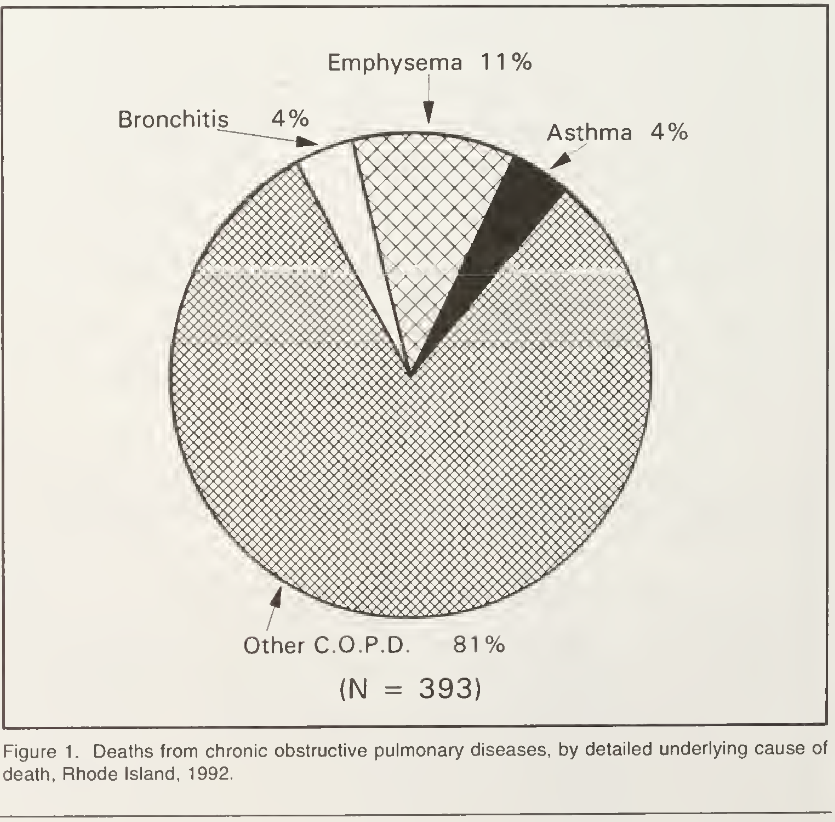

Figure 1. Deaths from chronic obstructive pulmonary diseases, by detailed underlying cause of death, Rhode Island, 1992.

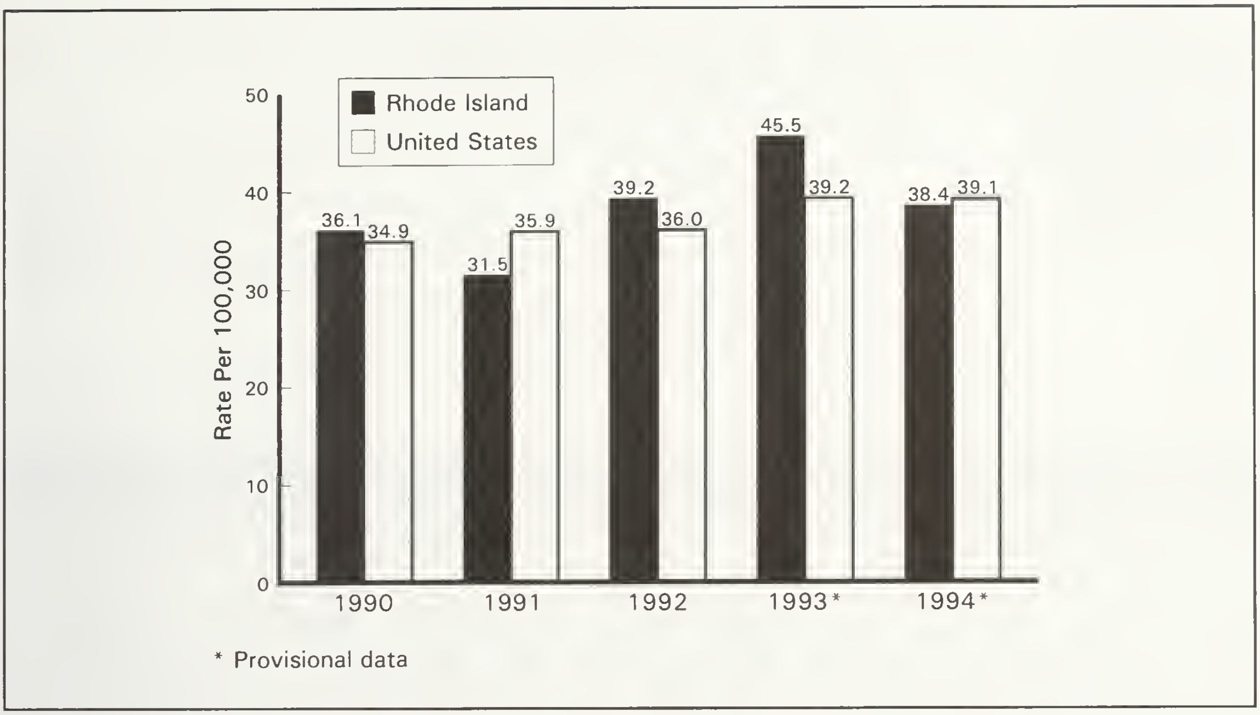

Figure 2. Mortality rate for chronic obstructive pulmonary disease, Rhode Island and United States, 1990-1994.

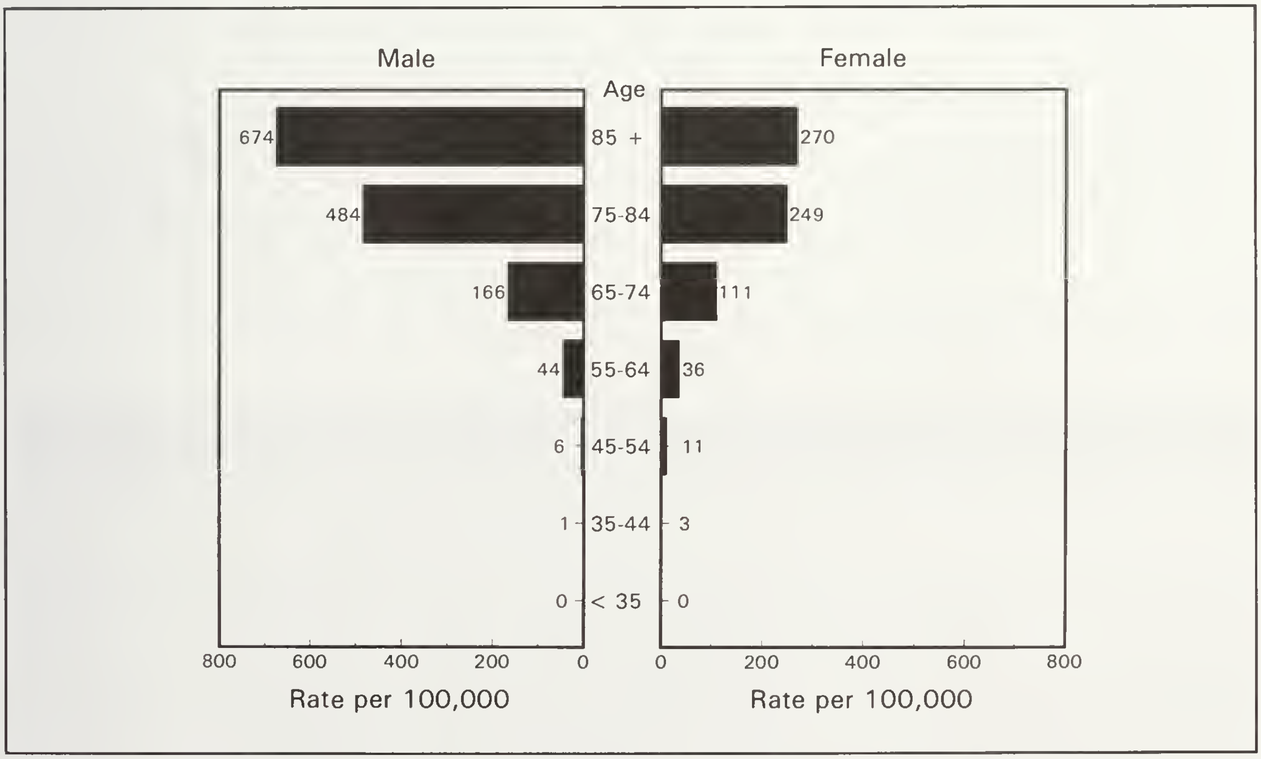

Figure 3. Mortality rate for chronic obstructive pulmonary diseases , by age group and sex, Rhode Island, 1992.

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Vital Statistics

Rhode Island Department of Health
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Edited by Roberta A. Chevoya

Rhode Island Monthly Vital Statistics Report
Provisional Occurrence Data from the Division of Vital Records

Vital Events

	Reporting Period		
	Sept 1995	12 months Ending with Sept 1995	
	Number	Number	Rates
Live Births	1,229	13,773	13.8*
Deaths	750	9,710	9.7*
Infant	(8)	(96)	7.0#
Neonatal	(7)	(76)	5.5#
Marriages	1,137	7,372	7.4*
Divorces	314	3,619	3.6*
Induced Terminations	473	5,834	423.6#
Spontaneous Fetal Deaths	92	1,032	74.9#
Under 20 weeks gestation	(89)	(964)	70.0#
20 + weeks gestation	(3)	(68)	4.9#

* Rates per 1,000 estimated population
# Rates per 1,000 live births

Underlying Cause of Death

	Reporting Period			
	March 1995	12 Months Ending with March 1995		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	290	3,249	326.1	4,409.0
Malignant Neoplasms	220	2,421	243.0	7,309.0
Cerebrovascular Diseases	55	593	59.5	759.5
Injuries (Accident/Suicide/Homicide)	24	339	34.0	6696.5
COPD	38	393	39.4	275.0

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.
(b) Rates per 100,000 current estimated population of 996,325.
(c) Years of Potential Life Lost (YPLL).

Note: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

THE RHODE ISLAND MEDICAL JOURNAL

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NINETY YEARS AGO

MARCH, 1906

The lead editorial expresses concern that the tragic fate of epileptic children, estimated to number 800 in Rhode Island, is not being addressed by society. The editorial notes that Rhode Island provides quite adequately for its "unfortunate and defective classes" except for the seizure-ridden children. "Even the autoist is to have good State roads for his pursuit..." The editorial concludes with a plea for the establishment of a Rhode Island State Home for Epileptics.

Frank B. Sprague, MD summarizes his experiences in the performance of one thousand adenoid operations. The etiology of the vast majority of cases, in his judgment, has not as yet been clarified but is perhaps "stimulated by constant irritation from particles of dust or secretions with mild infection." The diagnosis, he contends, is a simple matter and can often be recognized by the patient's facial expression, the mouth breathing, and the history of repeated upper respiratory infections. He then describes the preparation of the patient, the anesthetic, the positioning of the patient's body, and the operative technic. Lastly, he describes the complications, the personal results he has achieved, and the possibility of recurrence.

The epileptic and his treatment are described by George T. Spicer, MD. The article begins with an affirmation of the view of Hippocrates that the disease is not some divine judgment but rather a disorder arising from purely natural causes. He then decries the abandonment of the epileptic both by society and its physicians. He also condemns such older therapies as the bizarre therapeutic concoctions containing ground skull, macerated earthworms, the ashes of magpies and the dew gathered on the morning of St. John's Day. He then proceeds to talk about a more rational therapy, including attention to diet, the use of bromides to counter "the increased irritability of the nervous system" and the awareness of its side effects (bromism.) He then shares his experiences with an epileptic whose condition, initially, was "pitiable." But with tenacity and attention to detail, the patient, on 80 grains of bromide per day, is now gainfully employed, no longer suicidal and enjoying the pleasures of life.

FIFTY YEARS AGO

MARCH 1946

Herman C. Pitts, MD describes a plan for a voluntary surgical insurance program for Rhode Island, warning that we must take a mid-course between a "Tory complacency" and an unrealistic faith in "hasty experiments." He then outlines a preliminary plan involving Blue Cross, concluding that the success of this plan, as finally adopted, depends entirely on the attitude of the medical profession of the State. "If they accept it wholeheartedly as a public service, then it will steadily increase in usefulness and will become one more barrier erected by us opposed to the regimentation not only of ourselves but of the public, that is most certainly in the offing."

Thad Krolicki, MD discusses his experiences with the injection treatment of hemorrhoids. After considering background issues, the author then describes how cases are selected, the equipment needed, the injection technic and the advantages and disadvantages of the procedure. He concludes that in the majority of cases of external hemorrhoids, this procedure is satisfactory.

The medical care for veterans, the establishment of an augmented veterans administration medical division, and the future of a health care system for 20 million living veterans is discussed candidly by Major General Paul Hawley, the person in charge of Medicine & Surgery, US Veterans Administration.

The results of an opinion poll regarding "neuropsychiatric conditions among World War II veterans in Rhode Island" are provided by Hildegard Durfee, PhD.

The journal summarizes a new bill (HR 4717) recently signed by President Harry Truman, creating an enlarged Department of Medicine & Surgery in the Veterans Administration, with the aim of bringing its professional personnel into an organization comparable to the Army Medical Corps. Maximum salaries are: Chief of a service, $9,800. Junior grade physician, $4,300. Hospital attendants, $1,902 per year.

The yearly compilation of recorded communicable diseases in Rhode Island notes 407 cases of tuberculosis (69 deaths), 316 cases of scarlet fever (no deaths), and 34 cases of meningitis (3 deaths.)

The journal also rejoices upon the return to civilian life of 11 practitioners recently discharged from the military.

TWENTY FIVE YEARS AGO

MARCH, 1971

John Tierney, Assistant Director of Health, discusses the organization and delivery of health services in Rhode Island. After a detailed analysis, he concludes: " One way or another, we all sincerely desire the best possible health care for people."

A comparative study of the treatment of fractures of the shaft of the femur by traction and open fixation is presented by A.A. Savastano, MD and Eusebio Cadena, MD, based upon a retrospective analysis of 132 cases. They conclude that intramedullary fixation should be largely reserved for patients older than 22 years. Conservative traction treatment is their method of choice for the younger patient.

Robert Gorfine, MD describes the rare complication of acute perforation in regional enteritis, illustrating this with a detailed case report.

Arturo Longobardi, MD appraises the needle biopsy of the liver, emphasizing its value as a diagnostic tool.

Frances B. Sargent, MD, Richard Judkins, MD, Vittal Pai, MD, and Joseph Bellino, MD describe the effect of preoperative ingestion of Vitamin K_1 on prothrombin time.

Recent developments in Laser technology are offered by Leon Goldman, MD.

Robert V. Lewis, MD, while searching through the archives of the Redwood Library in Newport, found evidence that the eminent Benjamin Waterhouse had in his possession the original notes taken by Dr. James Brett, late of Newport, when he had been a student of Boerhaave at Leyden University. 1966 represented the 300th anniversary of Boerhaave's birth.

INFORMATION FOR CONTRIBUTORS

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A manuscript will be accepted for consideration with the understanding that is an original contribution, has never been published in its current form, and is submitted only to *Medicine and Health/Rhode Island*. An article should address a substantive issue of interest to the Rhode Island medical community, and be no more than 3,000 words in length and have no more than 20 references.

Submission Requirements

Manuscripts should be typewritten, double-spaced with liberal margins. Authors also are asked to provide the manuscript and computer-generated graphics on a floppy diskette, formatted in either Microsoft Word or Word Perfect. If possible, Macintosh disks should be saved in DOS format, using Apple File Exchange.

Illustrations and charts must be submitted in black ink on white paper. Laser-printed graphs are acceptable, provided they are printed at 300 DPI resolution.

Photographs must be in black and white, submitted on 5" x 7" glossy paper.

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Cover: A 19th century woodcut of an elder fleeing pain.

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COMMENTARIES

Cancer Pain

This year, more than one million Americans will be diagnosed with cancer, and almost half will have pain severe enough to significantly impair their quality of life. Unfortunately many, if not most of these patients, will not get satisfactory relief from their pain.

A recent Robert Wood Johnson Foundation study found that half of conscious patients who died in the hospital suffered moderate to severe pain in the final three days of life.[1]

This needless tragedy continues not because we await a scientific breakthrough in pain management, but because readily available medicines and methods are not being implemented. Little training in pain management, fears about addiction, concerns about opiate side effects, and scrutiny from regulatory agencies can all contribute to a physicians' reluctance to prescribe adequate medication to successfully treat pain.

Recognizing this problem, the Agency for Health Care Policy and Research published the Clinical Practice Guidelines for the Management of Cancer Pain. This was an important first step in a national effort to improve the treatment of cancer pain.

To enhance our statewide effort, this issue of *Medicine and Health / Rhode Island* is devoted to cancer pain management. The vast majority of cancer patients can get relief with simple, basic measures; however, radiation oncology and nuclear medicine can often provide relief to those patients whose pain cannot otherwise be controlled. For those patients who may have unacceptable side effects with opiates, these disciplines may provide another option.

The fear of regulatory scrutiny is often cited by physicians as contributing to their reluctance to prescribe opiates. We hope that the views and

ideas of the Department of Health, Division of Drug Control and the Board of Medical Licensure and Discipline presented in this issue will help to alleviate these fears. We also hope that they will serve to reassure physicians that well-documented, aggressive use of opiates in an effort to relieve cancer pain will be viewed with support and an understanding that we owe no less to our patients.

Edward W. Martin, MD

REFERENCE

1. The SUPPORT Principal Investigator for the SUPPORT Project. A controlled trial to improve care for seriously ill hospitalized patients: The Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT). JAMA. 1995;274:1591-1598.

Why Can't The Britons Learn to Speak English?

In his will establishing the scholarships which bear his name, Cecil Rhodes extolled the binding virtues of the English language which, he fervently believed, served to unify the English-speaking peoples. He was further convinced that English was the ideal instrument for administration, commerce, science and poetry. It was, he assured all, the agent which had helped to create a coherent, international organization chosen by circumstance to rule much of the world; and further, it was the vehicle which would bring Americans closer to their spiritual and linguistic roots in mother England. Little did he realize, in the words of Shaw, that England and America were in reality two countries divided by a common tongue.

The majority of Rhode Island's physicians, sooner or later, will visit England. As a small step in diminishing the anxieties that these colleagues might experience when encountering known words of unexpected meaning, the journal offers a brief narrative excursion employing some of these ambiguous words. The terms that British physicians might use are within parentheses.

> Shortly after arrival in London, despite being deeply fatigued [*knackered*] you visit a local druggist [*chemist*] to purchase some over-the-counter medications [*jollops*] specifically to treat a mild diarrhea [*gippy tummy*]; in addition, you seek some band-aids [*elastoplasts*], rubbing alcohol [*surgical spirits*], absorbent cotton [*cotton wool*], surgical bandage [*lint*], a hot water bottle [*stomach warmer*] and a pocket flashlight [*torch*]. You then pick up your rental car, placing all of your purchases in the trunk [*boot*], consult a map and proceed then to the appropriate highway [*arterial*] in order to drive to your host's office at the local school [*faculty*] of medicine. Years earlier, you and he had been fellow clinical clerks [*dressers*] and later residents [*registrars*] in surgery. Your friend has moved up within the British medical profession and is now a specialist [*consultant*] no longer making house calls [*domiciliaries*]. When you arrive at the private hospital [*nursing home*] where your friend is located, you seek out the information desk [*enquiry office*] first to request the location of the public bathroom [*public

convenience, WC, bog, loo] and then the location of your friend's office [*chambers*]. You fully realize that the next few hours will be devoted to the customary tour of the establishment, a visit to the OR [*surgical theatre*] and the inevitable introductions to the medical school dean [*principal*], faculty [*staff*] including instructors [*readers*] and professors [*lecturers*], the chief nurse [*matron*] and the staff nurses [*sisters*].

You have been warned that acronyms may also assume unaccustomed meanings in England. Thus, for example, STD does not signify sexually transmitted diseases but represents the acronym for long-distance telephone calls; and if you attend an AA meeting it is likely that you will learn more about flat tires [*tyres*] than sobriety.

There had been a time over a century ago when educated Englishmen, motivated by a spirit of high adventure, visited these shores to witness the unlettered natives as they mangled the lexicon and grammar of Standard English. A succession of writers, including Dickens and Trollope, toured American cities gathering data to document our curiously boorish neologisms and idiomatic phraseology. Even the writings of our educated were viewed disparagingly. *The Medical Times & Gazette* [London] in 1870, stated piously that ". . . the medical journals of the U.S. were written in a slang too outlandish and depraved for any decent English medical man to understand."

But where the words chosen by American physicians were once unerringly direct, aggressively brief and without embellishments, gradually they tended to have become more pretentious, polysyllabic and circumlocutious. Consider, for example, the lengthy, erudite names of many current American subspecialty medical journals; and then compare them with their refreshingly blunt British counterparts [the latter with names such as *Gut* or *Brain* or *Blood*.] Times have indeed changed and the colonials have become more English than the Brits. The frontier language of America is no longer visible while a conscious tilt toward simple Anglo-Saxon terms is now more a British than an American characteristic.

Linguistic bewilderment, of course, is a two-way street. Appreciate the astonishment of a Briton driving past some of the medical centers in Boston. He may confront a sign saying: "No Honking Allowed on Streets Near Hospital." Back in England, honking is their idiom for vomiting.

Yet there are still some in England who view with utter horror the American introduction of new words. Old believers regarded such barbarisms as seditious, if not immoral, acts of a philistine people who, ill-advisedly, were once allowed free use of the chaste English language. A letter to the London Times [November 1, 1974] expresses these grave anxieties: "Giving the English language to the Americans is like giving sex to small children; they know it is important but they don't know what to do with it."

Stanley M. Aronson, MD

A Stranger in Our Midst

The December, 1995, issue of *Nature* carried an article describing the morphology and life cycle of a newly discovered invertebrate species called *Symbion pandora*. It is a minute organism which adheres to the claws of the Norwegian lobster for most of its life, functioning mainly as a sessile asexual creature. But when the lobster molts its shell, the *symbion* – in order to survive – begins a brief but complex interval of sexual activity. It first extrudes a dwarf vesicle which in truth is nothing more than a free-living testis incapable of any metabolic activity other than short-term mobility and the eventual release of sperm. *Symbions* also bear an internal egg-bearing bud. The male dwarf seeks out another *symbion* and impregnates it. Thus every *symbion* harbors male and female gonads which are latent during lengthy intervals of unthreatened living. But in times of crisis, the male gonad is activated and, in the form of a virtually independent organism, undertakes extracorporeal wandering seeking another *symbion*. The female gonad, on the other hand, remains a passive stay-at-home.

The Latin *sexus* [from which is derived the word sex] is related to *secare*, meaning to cut, suggesting that the division between the genders is to be sharply and unambiguously defined. Intersexual or bisexual animals might be acknowledged in lower species but a human bearing basic male and female procreative elements is a puzzlement and is often not graciously accepted; this, despite the existence of such "intermediate" individuals in virtually all civilizations.

Ovid relates the poignant tale of Salmachis the nymph who falls passionately in love with a youth who swims in her mountain lake. He steadfastly resists her advances and she then appeals to the gods that she and this strange youth be eternally united. Zeus accedes to her wishes and, merged into one body which is both male and female, they sink forever beneath the waters. The youth's father was Hermes, son of Zeus and Maia, messenger of the Olympians, god of commerce and bearer of the caduceus; the youth's mother was Aphrodite, acclaimed goddess of love; and the youth's name, Hermaphrodite, was a fusion of the two parental names.

The intersexual creature was well known even before the Greeks formalized their lyrical cosmology. Nomadic shepherds have long recognized that when cows give birth to twins – a rare event – and when one calf is male and the other female, that the female will be sterile and will show masculine features, a creature with the outward features of both sexes.

True hermaphroditism, sometimes called simultaneous hermaphroditism, is defined as the coexistence of viable, mature ovarian and testicular tissues in the same adult organism. It is distinguishable from various forms of agonadism which represent neutered states with only minimal hormonal and morphologic features of the two sexes.

True hermaphrodites are usually chromatin-positive and with an XX chromosomal constitution.

A sea bass, *Serranus tortugarum*, living in the wild, may spawn eggs and within seconds, then release sperm. Marine biologists have now identified over 100 species of fish exhibiting yet another dramatic form of intersexuality called successive hermaphroditism. The usual succession is as follows: A female fish matures, lays eggs, then undergoes total ovarian atrophy followed by development of mature testes derived from some primordial cell clusters in her/his abdomen. In various species of the worm *Sagitta*, the germ cells within the middle segment mature into eggs while the tail section germ cells evolve into sperm. By various interventional stimuli, this order may be reversed thus confirming the totipotential nature of worm germ cells. The inquiring mind will inevitably wonder: Can these hermaphrodite species fertilize themselves? Yes, in worms; rarely in fish.

The angels of the androcentric Scriptures were described variously as cherubim [Gen 3:24], sons of God [Job 1:6] and as messengers [Daniel 3:28]. In an earlier context they were indisputably male with male names [eg, Michael, Gabriel, Raphael, etc.] Later angels became less defined, and often were nameless. Wesley was therefore of the opinion that they were genderless; this perplexed some and to others represented a trespass into forbidden territory. If the fusion of sexes were viewed as a freakish anomaly, a male-female angel would then become an object of derision; but, alternatively, if an angel were to represent a coalescence of both male and female forces, it may then be discerned as an object of fear. In neither case would the perception be angelic. Even Adam, before his rib resection, embodied both sexes.

About 0.3% of all living human beings are hermaphrodites, an estimated 750,000 in the world. And since intersexuality is frowned upon, to what sex should they be assigned? Roman Law states: "The sex of a hermaphrodite should be regarded as that which is apparently dominant, but in cases where the sex cannot be determined the Law shall take due regard of the circumstances which arise as a consequence of the uncertainty or lack of knowledge."

The human who is a hermaphrodite must bear a terrible burden. Society, and its laws and customs, has little tolerance for ambiguity; it insists that each citizen be of one sex or the other, much like the rigidity demanded in a two-party political system. Neither intersexuality, nor its social counterpart of transvestism, are happily tolerated. Genesis describes the creation of only two genders, and a rigid, dimorphic model has thus prevailed as the accepted norm; departures from this are construed by biologists as variations; by physicians as aberrations; and by a righteous few in society as abominations.

Stanley M. Aronson, MD

Down-sizing Time: Efficient But Hardly Effective

A doctor who cannot take a good history and a patient who cannot give one are in danger of giving and receiving bad treatment.

Paul Dudley White

In their greed for profit our managed-care masters, most of whom know little or nothing about medicine, are so bent on managing time that each patient visit is but a brief encounter. "I saw the doctor for only about eight minutes," my neighbor told me, and asked, after attributing this irritating visit to managed care, "Why aren't you doctors fighting back?'

The business crowd who have moved in on the practice of medicine cannot be blamed for doing what they have been trained to do: they know, until they get sick themselves, that the purpose of medicine is to make money. They know also that standards for diagnosis and treatment can be written, are being written, and can be made into computer programs so that with a few key strokes the physician can generate a diagnosis from which a treatment plan will be printed out. They betray their ignorance of human nature and history by being quite certain that preventive medicine will make expensive diagnosis and treatment rarely necessary. "Can't 85% of all diseases be prevented? That's what I've read. Why don't you doctors get on with it?" Anyway, prevention could be ladled out by a string of low-paid health-care workers, social workers, nutritionists, exercise therapists, acupuncturists, naturopaths, group therapists, counselors, sex therapists, and spiritual gurus. None of this will make a dent in the costs of "the health-care industry," but will vastly expand profit margins and market share.

Years ago, a brilliant clinical scientist, having listened to as much prevention talk as he could stand, commented, "Wear seat belts, don't get fat, don't smoke, have one or two drinks a day, no more, walk up two flights, down three, and get your flu shot. What else is there?" The receptionist, while taking your blood pressure, could tell you all that in less than eight minutes, and maybe pass out a tract on safe condom use or low-fact chocolate bars, or even low-fat fat.

William Mayo is reported to have said that "...the ideal medicine is to eliminate the need of a physician." This was Dr. Will's sentiment as an after-dinner speaker; as a surgeon he knew better. Preventing disease has, for the most part, been a byproduct of the industrial revolution, aseptic surgery, and the science of immunology. Even internists know that a world without surgeons would be a scary place indeed. We could stop worrying about population growth! And, by the way, AIDS is one of the most preventable diseases around and yet it is the major killer of young people, especially young men, and, world-wide, continues to roar right along.

It is time, more than anything else, that remains the essential element in the care of the sick and the worried well, and time it is that management wizards want to "down-size." Even in medical schools, students are taught to take a focused history, not a complete history, perform a focused physical examination, never mind asking about those things that matter to the patient, their jobs, their worries, their families, the world series, and the next election. The students' questions become stereotyped, and their manner patronizing as they ask a total stranger without looking up from the chart, "Well, Mary, what brings us to the clinic today?" After all, time is money, and Mrs. Mary Jones must be out and on her way to the lab in 10 minutes. No time to learn much about Mary. Teaching them how it will be in the real world, not how to change the world.

A professor of medicine told his house staff: "Take your time. Histories take time to unfold, and when they do, you're 90 percent along the way to a diagnosis and a plan." Another, a Regius Professor, said, "Let the disease declare itself if it's not obviously an emergency. You may not even need the lab!" Look again at Sir Zachary Cope's plan for the early diagnosis of the acute abdomen. An eight minute visit?

How much time is needed to feel and express sympathy, empathy, begin to care for the patient and show it?; how long to build a friendship, to be responsible *for* the patient, rather than *to* your friendly nurturing HMO?

Managed care, that is, managed care for profit, will, we pray, be a short footnote in medical history. If we don't bring it down, surely our patients will.

Robert U. Massey, MD

(from *Connecticut Medicine*, December 1995)

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Pharmacologic Management of Cancer Pain

Edward W. Martin, MD

Cancer pain can be effectively relieved in up to 90 percent of patients with the simple, systematic use of available oral medications. Many patients, however, endure uncontrolled pain because these medications are not prescribed or are not prescribed in doses and schedules adequate to relieve pain. This review will outline an approach to the treatment of cancer pain using readily available medications, focusing primarily on opiates.

Pharmacologic therapy is the primary intervention in managing cancer pain. Mild pain may respond to acetaminophen or nonsteroidal anti-inflammatory drugs given on a regular basis. Some studies have noted particular efficacy of nonsteroidals for bone pain. Moderate or severe pain, however, cannot be controlled without the use of opiates.

The World Health Organization has recommended morphine as the drug of choice for cancer pain. This is the most commonly used opiate for moderate or severe cancer pain. It is generally preferred due to its availability and multiple dosage forms, including immediate release, which is available as both liquid and tablet, sustained release in tablet form for oral use, and suppositories. Some physicians, however, are reluctant to prescribe morphine and other opiates for their patients with cancer pain. Some patients also may be reluctant to take morphine. This may be due to a number of misunderstanding regarding morphine, related to the myths about this drug which are so prevalent in our society:

Myth #1: Morphine dosage cannot exceed the maximum.

Morphine and the other pure opiate agonists have no maximum dose. The drug can be increased to a level needed to achieve analgesia while monitoring for side effects.

Myth #2: Patients rapidly become tolerant to morphine and require continually increasing doses.

Tolerance is generally not a clinical problem. Increasing dose requirements are usually due to disease progression. Stable patients may remain at the same dose for weeks or months. In cases where tolerance to the analgesic effect does develop, the dose can be increased until pain control is achieved.

Myth #3: Morphine causes addiction and must be used with great restraint.

Addiction to opiates is rarely a problem in the clinical management of cancer pain. All patients taking opiates will develop some degree of physiologic dependence if the dose and duration of therapy is sufficient. This is not addiction. Just as patients on high dose steroids may become physiologically dependent on exogenous steroids, so too, do patients receiving opiates. Given this, opiates must not be stopped precipitously.

Myth #4: Morphine should be reserved for the final stages of illness or it will lose its effectiveness.

This is a common misunderstanding. Unlike antibiotic therapy, resistance does not develop. Increasing doses of morphine will provide increasing analgesia if needed, as the disease progresses. There is no reason for morphine to be withheld to preserve its efficacy.

Myth #5: Morphine causes respiratory depression and should be avoided in patients with lung disease.

Tolerance develops quickly to the respiratory depressant effects of morphine; and as used in cancer pain management, this has not been a significant clinical problem. Of note, morphine is used clinically to reduce dyspnea in patients with cancer.

Myth #6: Patients who require more frequent administration or increasing doses of morphine, or develop pain while on morphine, are becoming addicted.

Disease progression, inadequate dosing, and individual variation in the half-life of morphine are the primary reasons patients on morphine continue to experience pain.

Myth #7: Parenteral administration is more effective than oral morphine.

Morphine must be dosed differently when given orally due to first-pass hepatic metabolism. But the ease of administration, lower cost, increased patient control, and stable levels make the oral route preferred.

Myth #8: The patient will be walking around like a zombie.

Dr. Jack Khvorkian has stated that this is the reason some patients have sought his assistance rather than pain relief. Sedation is common initially, but tolerance to this develops quickly. Most patients on morphine are up and about with minimal sedative effects.

Morphine and opiates do have a number of side effects, and an understanding of these is essential for a clinician to use opiates effectively. The prevention and management of side effects is critical if the opiates are to be titrated quickly to analgesic levels. A patient who is not educated regarding the side effects is much less likely to comply with a regimen which will provide analgesia.

Respiratory depression is the side effect most feared by clinicians. In fact, this is rarely a problem clinically in managing cancer pain, since morphine is titrated to achieve pain relief. Tolerance to respiratory depression develops quickly.

Nausea and vomiting are common symptoms in patients starting opiate therapy. Many patients report they are "allergic" to various opiates after having experienced nausea and vomiting with previous administration. Opiates directly stimulate the chemoreceptor trigger zone in the medulla. Some patients may require an anti-emetic when beginning opiate therapy, especially if they have a history of this problem. It is helpful to advise patients to limit activity for the first few days on opiates, since activity will increase the vestibular contribution to nausea. Fortunately, most patients rapidly develop tolerance to this side effect as well.

Sedation is very common and generally subsides as tolerance develops over several days. In those patients who continue to experience sedation from opiates, methylphenidate (Ritalin) can be added to increase alertness.

Constipation develops in virtually all patients, and most do not develop tolerance to this side effect. Patients started on opiates must be started on a bowel regimen. Cancer patients also may have other risk factors for constipation, such as a change in diet and a reduction in activity level. Patients may require several agents such as stimulating cathartic; i.e., a senna preparation or bisacodyl and an osmotic agent such as sorbitol.

Myoclonus can be alarming to patients and families who may feel this is seizure activity. Reassurance that this does not represent a seizure is often an adequate intervention, but more bothersome episodes can be ameliorated with benzodiazepines.

Pruritus, due to the release of histamines by morphine, can be controlled with antihistamines. In more severe cases, other opiates such as hydromorphone (dilaudid) or fentanyl (duragesic) are less likely to cause pruritus.

Urinary retention is more common in older patients and is usually transient.

Confusion may be noted in patients, particularly at the beginning of opiate therapy. This is usually transient. Low doses of haloperidol (haldol) may be helpful. At times, a change in opiate may result in a decrease in confusion.

MANAGING TREATMENT

Once it has been determined that a patient will require opiates for pain management, a few general principles apply. The medication should be dosed on a schedule to maintain a steady blood level. The objective is to avoid troughs in drug levels at which time the patient would experience pain and to avoid peaks, when increased side effects might be noted. This is often counter-intuitive for patients and families who are used to taking pain medications only when they have pain.

Medication should be titrated up expeditiously. There is no reason to allow a patient to suffer for days in pain, awaiting the next dose increase. In titrating oral morphine, the dose should be reviewed daily and increased as necessary until pain control is achieved.

When titrating opiates, dose increases should represent a percentage of the total daily dose; i.e., 25-50%. For example, a patient getting 10 mg every four hours might benefit from an increase to 15-20mg every four hours. For a patient receiving 100mg every four hours, a 5-10mg dose increase is unlikely to be effective.

Addiction to opiates is rarely a problem in the clinical management of cancer pain.

The oral route is preferred for patients able to take their medications by mouth because of the convenience and simplicity of its administration. While first-pass metabolism is considerable, with proper dosing, effective blood levels can be readily achieved with oral administration.

When the total 24-hour morphine requirement is determined, the patient can be switched from an every 4-hour schedule to a twice per day schedule with sustained-release morphine. This improves compliance and avoids requiring the patient to take medication in the middle of the night or be faced with pain upon awakening. The dose of morphine taken in 24 hours is simply divided by two and administered twice per day. For example, a patient getting 60mg every four hours (360mg over 24 hours) would receive 180mg of sustained-release morphine twice a day. There is no reason to give the sustained-release preparations more often than twice a day.

Patients should continue to have some immediate-release morphine available in the event of breakthrough pain. The sustained-release morphine is not appropriate to use in this way. Patients will generally need a dose equivalent to about one-third of their twice per day dose for breakthrough. For example, a patient getting 300mg twice a day will require 100mg for an effective breakthrough dose.

Opiates, especially when used in higher doses for prolonged periods, should never be stopped abruptly. If the source of pain is removed, i.e., secondary to therapy, the drug can be tapered gradually then discontinued. This should avoid withdrawal that can be uncomfortable and frightening.

When frequent breakthrough doses are needed, the sustained-release dose should be increased. For example, a patient getting 200mg every 12 hours, who receives four breakthrough doses of 60mg, should have the sustained-release dose increased to 320mg every 12 hours and the breakthrough dose increased to 100mg. Ongoing reassessment and titration are essential to achieving optimal pain control.

Equi-analgesic tables should be consulted when changing from one opiate to another or when changing routes. For example, the parenteral dose of morphine is one-third of the dose given orally.

There is no reason to combine multiple opiates. Unlike many of the cytotoxic drugs used in chemotherapy, opiates have nearly an identical side effects profile. No advantage is gained by using multiple opiates. There is no rationale for combining sustained-release morphine and transdermal fentanyl.

The transdermal fentanyl patch (duragesic) is ideal for patients who cannot take medication orally or prefer transdermal systems. It is generally indicated for patients who are stable, since it is not a titratable drug.

Some opiates are not recommended for use in the management of cancer pain. Meperidine (Demerol) is metabolized to normeperidine. The metabolite accumulates with repeated administration and can lead to central nervous system toxicity, including tremors and seizures. It has the shortest half-life of the opiates and so its brief duration of action, two to three hours, makes it a poor choice for the cancer patient with pain.

Mixed agaonist-antagonists such as pentazocine (Talwin), butorphanol and nalbuphine have an analgesic ceiling and may precipitate withdrawal when given to a patient on other opiates. Brompton's mixture, popular years ago, contained morphine and other drugs in an elixir. The ingredients varied and it was found to have no advantage over morphine alone in treating pain.

Adjuvant drugs may be helpful with particular pain syndromes and may enable the achievement of good analgesia with a lower dose of opiates.

Tricyclic antidepressants are particularly beneficial in patients with neuropathic pain. These drugs have the added benefit of treating depression, a common problem in cancer patients. They also are mildly sedating which can aid sleep when given at bedtime. Nortriptyline has less anticholinergic side effects than amitriptyline and is generally well tolerated. Nortriptyline can be started at a low dose, i.e., 10mg at bedtime and titrated up to 50, 100, or150mg at bedtime.

Anticonvulsants have been used as adjuvant therapy in cancer pain, particularly in lancinating neuropathic pain. Carbamazepine (Tegratol), phenytoin (Dilantin), and clonazepam (Klonopin), have been used, often with limited success. Mexiletine also has been used in neuropathic pain syndromes.

Corticosteroids are an underutilized adjuvant in cancer pain management. In addition to reducing nausea, increasing appetite and a sense of well-being, corticosteroids can be a useful adjuvant in cancer pain, especially in a patient with bone pain.

In some patients, an oral route simply will not be the preferred route of administration. Most patients in the final stages of their illness will be unable to take medications by mouth, and for most of these patients, suppositories can be used to maintain analgesia. Patients with an unstable pain syndrome and who are unable to tolerate oral medication may benefit from a continuous infusion of opiates, usually morphine or hydromorphine (dilaudid). The same principles of titration apply, increasing doses until pain control is achieved while monitoring for side effects. A pump allows the opiates to be infused continuously. Additionally, patients can self-administer bolus doses for breakthrough pain. A daily assessment continues with the hourly dose adjusted based on the number of boluses used in the preceding 24 hours. The infusion may be delivered subcutaneously or, if access is available, intravenously.

The vast majority of cancer patients with pain could achieve pain relief with an effective program of oral medications. Patients deserve no less than a comprehensive, systematic approach to pain relief, which could eliminate tremendous suffering.

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Interventional Management of Cancer Pain

Frederick W. Burgess, MD, PhD

Pain is a common symptom accompanying the initial diagnosis of malignancy. Estimates from the World Health Organization indicate that 20-50% of patients diagnosed with cancer will initially seek medical attention with a complaint of pain.[1] On average, 75% of cancer patients with advanced disease will experience moderate to severe pain. Of those reporting pain, 40 to 50% will complain of moderate to severe pain, while another 25 to 30% will report severe pain.[2] Estimates indicate that 90% of these individuals' pain can be readily controlled with conventional therapies, including oral analgesics, chemotherapy, radiation, and adjuvant analgesics. Unfortunately, the remaining 10% will continue to experience unremitting pain refractory to conventional therapy, or suffer unacceptable side effects limiting their acceptance of analgesic medication.[3] This review will focus on current and developing interventional treatments for cancer pain refractory to conventional pain management techniques.

Patients who have exhausted their options for pain control with chemotherapy, radiation therapy or surgery will require an aggressive analgesic approach involving systemic opiates, nonsteroidal antiinflammatory agents, occasionally steroids, and other analgesic adjuvants. Oral opiates continue to be the mainstay in cancer pain management. Oral opiates offer a considerable margin of safety, low cost, ease of administration, and simplicity of dose adjustment. Most patients with nociceptive pain will respond well to opiate therapy; however, for some individuals, opiate related side effects may limit patient acceptance. While opiate induced constipation and nausea can be controlled in the majority of patients, marked sedation, dysphoria, and hallucinations are difficult to overcome. In addition, dysesthetic sensations and neuropathic pain are often poorly responsive to opiate therapy. Adjuvant medications for the treatment of neuropathic pain, including antidepressants, anticonvulsants, and systemic local anesthetics, have a therapeutic ceiling limiting their efficacy. They also produce additional unwanted side effects, including sedation, dry mouth, nausea and vomiting, and impairment of hematopoiesis.

Under what circumstances should the treating physician consider pursuing an invasive approach to cancer pain management? The clinical practice guidelines for Management of Cancer Pain, 1994, recommend exhausting all noninvasive options.[4] According to the guidelines, failure to obtain adequate analgesia, intractable side effects, and the availability of skilled specialists in the area of anesthesia/pain management and neurosurgery are indications for proceeding with invasive pain management techniques. Indications for invasive pain control measures should include localized or regional distribution of pain symptoms. Examples of these indications are local chest wall invasion by intrathoracic malignancies, rib metastases, thoracic spine metastases, abdominal or pelvic visceral pain sources, and lumbar, sacral, and brachial plexopathies. Most unilateral pain syndromes, excluding plexopathies, can be effectively treated with neurolytic peripheral or central nerve blocks. Patients with life expectancies of three months or less are very effectively managed with neurolytic nerve blocks. In skilled hands, these block have a low incidence of complications, are minimally invasive and well tolerated, and can help to reduce opiate requirements, and ultimately reduce side effects resulting in an improved quality of life. Patients with plexopathies are infrequently considered for neurolytic blocks, since most patients don't tolerate numbness in their extremities well and may suffer motor weakness. In this population, a neurosurgical approach, such as a percutaneous cervical cordotomy or thalamic lesioning may prove very beneficial.

NEUROLYTIC NERVE BLOCKS

Contrary to popular misconception, neurolytic nerve blocks are not permanent. The duration of neurolytic block depends on the nature of the pain, the particular nerve treated, and the neurolytic chemical applied. Typically, benign pain responds with a fairly prolonged effect, while many cancer pains will exhibit an effect of shorter duration. In most patients, the effect of a neurolytic peripheral nerve block, e.g., an intercostal nerve block, may last from two weeks to two months. A celiac or superior hypogastric plexus neurolytic block may persist for up to six months.[5] Smaller nerve fibers and branches are more profoundly affected by the neurolytic agents and will often provide a more sustained effect. The often reversible nature of neurolytic blocks is advantageous should undesired motor effects develop, or impairment of bladder function occur due to excessive spread of the neurolytic agent. Furthermore, most neurolytic blocks can be repeated at needed intervals to compensate for extension of the malignancy or neural regeneration. Examples of various neurolytic blocks and their indications are listed in Table 1.

The most commonly applied neurolytic agents include phenol, ammonium chloride, and alcohol. Phenol has become the most widely used neurolytic agent. It has the advantage of having local anesthetic properties, thus, it can be applied without causing pain or requiring the concomitant use of a local anesthetic, which may dilute the neurolytic agent and contribute to excessive spread of the agent. Also, phenol has a lower risk of producing a chemical neuritis, which is more commonly associated with the use of alcohol. Other potential complications of neurolytic blocks include skin necrosis with superficial nerve blocks, risks associated with needle placement, and undesired spread of the

ABBREVIATIONS USED

CSF	Cerebrospinal fluid
TENS	Transcutaneous electrical nerve stimulation

chemical to surrounding healthy tissues producing organ or nerve damage. An experienced operator, the use of small volumes, repeated injections, and the use of fluoroscopic guidance can greatly reduce the risk of complications.

CENTRAL NEURAXIS OPIATES

Patients experiencing excessive sedation, neuropathic pain secondary to plexus invasion, or inadequate analgesia with conventional therapy should be considered for an epidural or subarachnoid opiate delivery system. Epidural and subarachnoid opioids are now widely employed in acute postoperative pain management. They offer the advantage of longer duration, lower total opiate exposure, more intense analgesia, and less sedation.[6] Furthermore, dilute local anesthetics may be combined with the opiates to provide improved analgesia, particularly with neuropathic pains (plexopathy).[7] It is important, however, to recognize that these techniques are a potential source of infection, and should not be inserted into an infected patient or into a patient with an uncorrected coagulopathy. Central neuraxis opioids will produce side effects, such as constipation, urinary retention, pruritis, and nausea and vomiting, common to systemic opioids.

It is also important to recognize that pain originating above the diaphragm will be more difficult to control with opiates administered at the lumbar level. Cerebral spinal fluid (CSF) tends to flow out from the choroid plexus, thus an opioid administered into the lumbar region must diffuse against a CSF current. Although the spinal opioids do reach significant levels in the cervical area, the spread can be slow and erratic. Administration of the opioids close to the spinal segment involving the region of pain can provide a segmental analgesic effect, especially when combined with a local anesthetic. This may be obtained with epidural catheters, but it is usually not technically feasible or desirable for subarachnoid delivery. An alternative approach involves the insertion of a catheter into the lateral ventricle for the periodic injection of morphine. This technique works very well for patients with head and neck malignancies and, surprisngly, does not promote marked respiratory depression.

The selection of a particular epidural or subarachnoid opioid delivery system is primarily determined by the anticipated longevity of the patient and the opiate requirement. Individuals requiring very high doses of opiate will do better with a subarachnoid catheter. Adequate analgesia can usually be obtained with 1/100th of the systemic morphine dose administered into the subarachnoid space, potentially reducing systemic opiate side effects. Epidural doses are usually 1/7th to 1/10th the current systemic morphine dose. Only 3-5% of an epidural dose will cross the dural barrier into the spinal fluid.[6]

> *Patients who have exhausted their options for pain control with chemotherapy, radiation therapy or surgery will require an aggressive analgesic approach involving systemic opiates, nonsteroidal anti-inflammatory agents, occasionally steroids, and other analgesic adjuvants.*

Terminal patients expected to live less than three weeks, will often do well with a standard temporary percutaneous catheter. Most temporary catheters will function well, if not dislodged, for 2-3 weeks. This approach is minimally invasive, does not require surgery or sedation, and can be inserted at the bedside in most situations. Individuals anticipated to survive for 1-3 months should have a tunneled percutaneous catheter inserted, similar to a Hickman catheter (DuPen; Bard), or a totally implantable subcutaneous port. Percutaneous catheters have a slightly higher risk of infection, usually involving the insertion site, but are often more comfortable for the patient because they do not require frequent skin punctures. Patients with a greater than three month survival are better managed with a totally implantable subarachnoid system, such as the Medtronic programmable SynchroMed infusion system, or an Infusaid pump.[8] These devices, while more costly at the start, ultimately reduce nursing related costs, cannot be dislodged, and carry a lower risk of infection, since they need to be refilled only at six weeks to two month intervals. Furthermore, epidural devices have a limited period of function. In many patients, a fibrotic sheath develops around the epidural catheter, interfering with distribution of the drug into the cerebrospinal fluid. Fortunately, most insurers will cover the costs associated with epidural and subarachnoid delivery systems, which in some circumstances will prove to be less expensive for the patient who must pay for their own prescription medications, provided that all noninvasive options have been exhausted and prior approval is obtained.

Almost any opioid may be administered epidurally. However, morphine continues to be the most widely used, due to its relative hydrophilic properties, which provide a long duration of action, and its low cost.[6] Preservative-free hydromorphone is a useful alternative with similar properties, but may have less pruritis associated with it. Whichever opioid is selected, care must be taken to insure that it is preservative-free. Many opioid preparations incorporate neurotoxic substances as preservatives, including formaldehyde, phenol, and methylparaben.

ON THE HORIZON

Although the use of central neuraxis opiates and neurolytic blocks can be very efficacious at managing difficult pain situations, they are prone to malfunction, contamination and infection, and may require repeated treatments (refills or repeat blocks). The ideal approach would involve the use of a potent analgesic agent or combination of agents, and a continuous, self-renewing delivery system. One approach to this problem is the concept of neuromodulation. The nervous system contains a number of inhibitory pathways capable of modulating the amplitude of nociceptive stimuli. The efferent activity of these inhibitory pathways may fail or be inadequate to control the painful implulses generated by the malignant tissue. Thus, the administration of exogenous opioids, such as morphine or fentanyl, supplements the native substrates (metenkephalin or the endorphins) at the inhibitory recep-

Table 1
Common indications for neurolytic blocks

Chest wall invasion	Intrathecal, epidural Interpleural Rib blocks
Thoracic spine mets	Epidural Spinal
Liver; colon; pancreatic tumors	Celiac plexus
Pelvic malignancy	Superior-hypograstic-plexus block

tor (the opiate receptors). Techniques to stimulate the activity of the endogenous opiate effector pathways include the administration of heterocyclic antidepressants, e.g. amitriptyline, and the use of neurostimulation (TENS or spinal cord stimulation). Although these techniques are often helpful in the management of benign pain conditions, they rarely provide adequate control of cancer pain.

An alternative approach involves amplifying the activity or increasing the number of inhibitory neural effector cells. This may be accomplished by transplanting additional neural tissue into the central nervous system. A seemingly unrealistic approach at first look, may now be closer to becoming a practical reality. Animal models have demonstrated that transplantation of adrenal chromaffin cell suspensions into the subarachnoid space is effective at controlling the behavioral response to acute and chronic pain.[9,10] Adrenal chromaffin cells produce a variety of neuroactive and analgesic substances, including metenkephalin, neuropeptide Y, epinephrine, and norepinephrine. Metenkephalin is believed to be the predominant inhibitory neurotransmitter in the dorsal horn of the spinal cord. Activation of the inhibitory pathways regulating the liberation of metenkephalin appears to be under the influence of spinal and brainstem noradrenergic neurons; hence the possible contribution of epinephrine and norepinephrine at the alpha-2 adrenoreceptor mediated analgesic response.[11]

Recently, this approach has been adapted to human cancer patients producing substantial, and in several patients, a complete elimination of the need for opiate analgesics, extending up to the time of death.[12] In this study, human allogeneic adrenal cells were harvested from organ donors, the chromaffin cells were isolated in tissue culture then injected into the cerebral spinal fluid in the lumbar subarachnoid space of five volunteers with end stage malignancies. To prevent rejection, systemic immunosuppressive therapy was administered in conjunction with these initial transplants; however, the investigators have suggested this may not be necessary. Three of the five subjects demonstrated a progression of improved pain control and the elimination of opiate analgesics over a 30-60 day period. The remaining two patients displayed a less dramatic response.

The difficulty in obtaining an adequate and reliable supply of organ donors, the risk of transmitting viral infections, and the use of immunosuppression will likely limit the widespread acceptance of this approach. An alternative solution to these problems may be provided by encapsulating adrenal chromaffin cells from xenogenic sources or cultured cell lines inside an implantable barrier membrane, eliminating the need for immuno-sup-pression and reducing the likelihood of transmitting infection. CytoThera-peutics, a Rhode Island based company, has developed a biologically inert encapsulation system that provides a mutually protective barrier preventing direct contact between the host and transplanted tissue. Nutrients and pharmacologically active molecules, including small proteins and peptides, are capable of diffusing freely through the barrier to sustain cellular metabolism and allow the flux of the metabolic substrates. Currently, Phase I clinical trials using this device (CereCRIB, 1.0; CytoTherapeutics, Inc.), containing bovine adrenal chromaffin cells, are underway in Switzerland and in the U.S. at Rhode Island Hospital.[13] A schematic of the device is shown in Figure 1. The implant is inserted via an introducer system into the subarachnoid space, requiring only a small subcutaneous incision performed under local anesthesia. The value of this approach is that it is a continuous delivery system and does not require replenishment. The adrenal cells are a self-renewing drug delivery system. Preliminary assessments on the efficacy of these devices have been encouraging; however, rigorous evaluation in blinded clinical trials will be necessary for general acceptance.

Greater awareness of the problem and the availability of improved treatment modalities has improved the quality of life for many cancer pain patients. Still, many patients will continue to suffer from poorly controlled pain secondary to opiate insensitive pain or intolerable side effects associated with the use of opioid analgesics. Invasive approaches to control cancer pain are available, but are often not offered to patients until very late in the process. Earlier application of intrathecal opiates, neurolytic blocks, and in the future, cell transplant therapy may im-

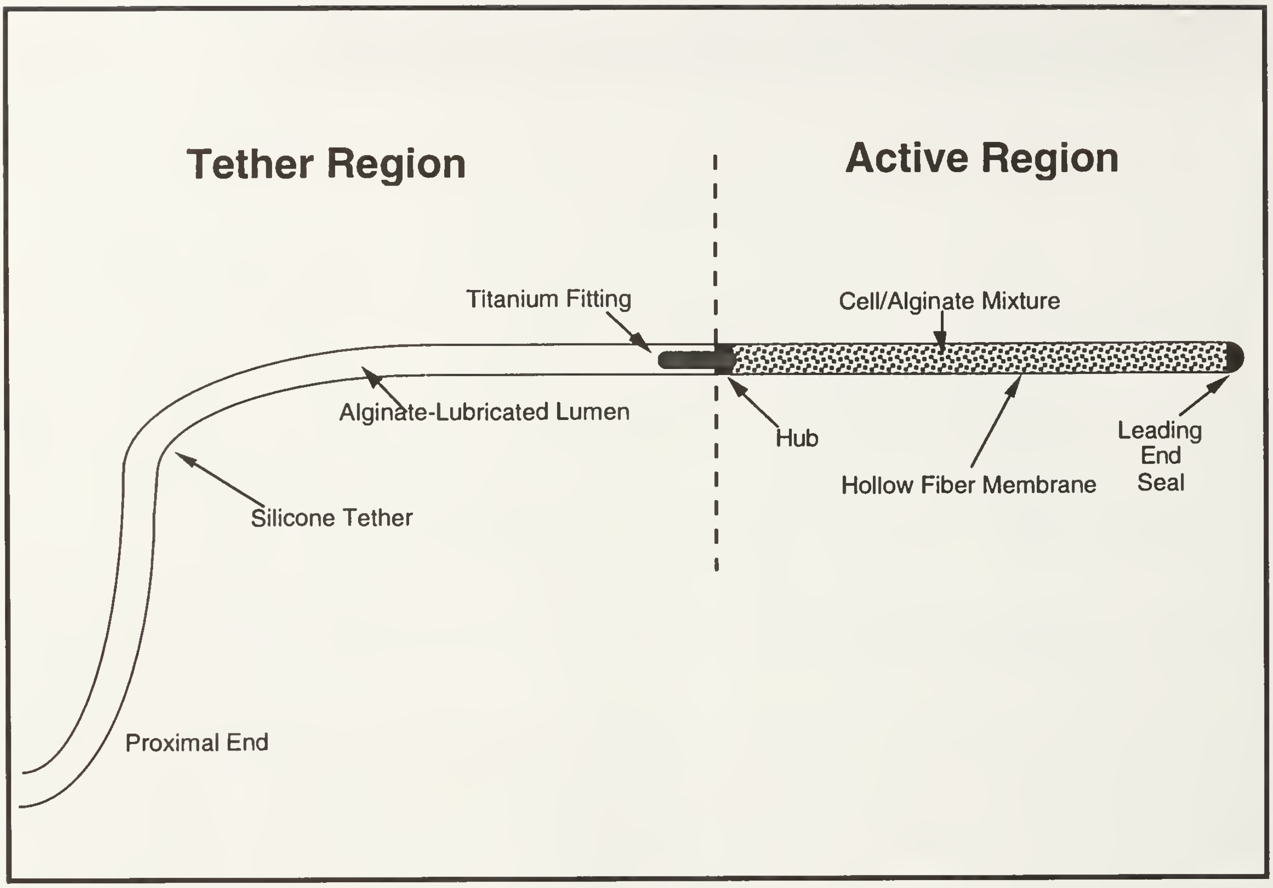

Figure 1. Schematic diagram of the CereCRIB 1.0 adrenal medullary cell implant for cancer pain control.

prove pain control, function, and quality of life.

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The Role of Radiation Therapy in the Management of Bone Metastases

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Metastatic cancer is the most common malignant neoplasm involving the skeletal system. Of the nearly one million new cancer patients diagnosed this year in the United States, approximately one-half will develop bone involvement at some point in the course of their illness. For a significant proportion of these patients, bone metastases will cause significant morbidity and suffering. Complications arising from bone involvement include severe pain, pathologic fractures, spinal cord compression, and hypercalcemia. Prompt identification of bone metastases and a complete assessment of sites of involvement should lead to rapid institution of appropriate palliative therapies. This will often delay or prevent functional deterioration and avoid some of the complications listed above.Therapy for bone metastases requires a multimodality approach that combines the skills of the medical, surgical, and radiation oncologists. This review will focus primarily on the role of radiation therapy in the treatment of bone metastases at various anatomic sites. The importance of radiation therapy (RT) in this setting cannot be underestimated.

Depending on the primary site of cancer, over three-fourths of patients undergoing RT will obtain moderate to good pain relief with a substantial proportion achieving complete relief.[1] Those who experience a good palliative response invariably will see an improvement in functional status and a decrease in pain medication requirements.

Ultimately, the decision whether or not to give palliative RT should be based on the following factors: 1) the patient's wishes, 2) severity of symptoms, 3) expected survival time, 4) likelihood of response, 5) severity and length of side effects; and 6) cost/benefit ratio.

The overall aim of palliative radiotherapy for metastatic cancer is always to improve the quality of life of the patient. Treatment success or failure should be measured accordingly.

ABBREVIATIONS USED

CT	Computed tomography
GI	Gastro-intestinal
IV	Intravenous
MRI	Magnetic resonance imaging
RT	Radiation therapy
RTOG	Radiation Therapy Oncology Group
TNF	Tumor necrosis factor

INCIDENCE AND ANATOMIC SITES

Although bone metastases have been reported in virtually all malignancies, the leading tumor types associated with osseous involvement include breast, lung, and prostate cancer. These three malignancies alone account for at least 80 percent of cases of metastatic bone cancer.[2] Other carcinomas, such as kidney and thyroid, also have a high incidence of bone metastasis, but account for a smaller percentage of lesions because of their low prevalence. In Table 1, the incidence of skeletal metastases in collected post mortem studies is summarized.[3] The distribution of bone metastases is primarily to the axial rather than the appendicular skeleton. The pattern of involvement of most tumors appears similar. Certain cancers, however, do have a predilection for certain sites, such as prostate cancer to pelvic bones. In a study by Clain, analyzing a group of 2,000 patients who died of various cancers with bone metastases, the breakdown of sites of involvement was as follows: Vertebra 69%; pelvis 41%; femur 25%; and skull 14%.[4] It should be noted, however, that virtually any bone can be involved with tumor.

MECHANISMS AND PATHOGENESIS

The way in which tumor cells migrate to the skeletal system and establish metastases, their relationship to the primary tumor, and the way in which they destroy normal bone are poorly understood. There are vascular and microvascular considerations as well as direct and indirect relationships of tumor cells to bone.[5]

Bone is comprised of complex tissue. Its formation and destruction is dependent on the function of three main types of cells: the osteoblast, the osteoclast, and the osteocyte. Normal bone does not contain any lymphatic channels. Skeletal metastases are usually seeded by hematogeneous spread. Early experiments by Batson in animals and human cadavers demonstrated the presence of a vertebral-venous plexus. This system runs parallel, joins, and can also bypass the other three venous systems and provides a pathway for the spread of disease between distant organs.[6,7] These experiments led to the understanding of the frequency and distribution of metastases along the vertebral column and limb girdle such as is commonly seen with prostate and breast cancer. The predominant distribution of bone metastases in the axial skeleton in which most of the red bone marrow is situated, suggests that the slow blood flow at these sites may assist in the attachment of metastatic cells, while its unique cellular structure contributes to the propensity of tumor cell extravasation and formation of metastatic foci.[8] Local factors produced in the bone environment can favor tumor growth or migration and it is known that cells of the bone are capable of producing a variety of different regulatory and growth factors. The matrix of the bone contains many factors, such as fibroblast growth factor, platelet derived growth factor, transforming growth factor-beta, and insulin-like growth factors 1 and 2, each of which, under appropriate circumstances, may function as growth factors for tumor cells.[9]

The mechanisms by which tumor cells destroy bone are complex and involve both direct and indirect mechanisms. Tumor cells may directly resorb bone. They may also produce substances such as parathyroid hormone-related protein, transforming factor alpha and beta, prostaglandins of the E series and cytokines such as Interleukin 1 and 6, as well as TNF alpha and beta which stimulate osteoclastic activity resulting in lytic bone lesions.[10]

An additional mechanism involves stimulation of new bone formation

Table 1
Incidence of Skeletal Metastases in Autopsy Studies

Primary Tumor Site	No. of Studies	Incidence (%) of Bone Metastases Median	Range
Breast	5	73	47-85
Prostate	6	68	33-85
Thyroid	4	42	28-60
Kidney	3	35	33-40
Bronchus	4	36	30-55
Esophagus	3	6	5-7
Gastrointestinal tract	4	5	3-11

Data from Galasko[3]

through increased osteoblastic activity. This is frequently seen in patients with prostate cancer. Both lytic and blastic lesions may cause pain and destroy the structural integrity of bone. In patients with extensive, destructive metastatic lesions, hypercalcemia is frequently present. This is particularly common when the kidneys' ability to excrete calcium is impaired (e.g., multiple myeloma).

DIFFERENTIAL DIAGNOSIS

Metastatic involvement of the skeleton typically affects multiple sites and causes pain with bony tenderness and increasing functional disability. The diagnosis is often straight-forward, but occasionally can be difficult to make with certainty. Confusion with benign lesions is particularly difficult in elderly patients in whom degenerative disease and osteoporosis are common findings. This is seen in elderly women with a history of breast cancer in whom it can be difficult to distinguish osteoporotic collapse from metastases. It can also be difficult to make the diagnosis in elderly men with prostate cancer where pelvic pain and sclerotic changes could be attributable to either metastatic disease or Paget's disease of bone. A primary sarcoma of bone may occasionally be mistaken for a solitary metastatic deposit. There are other bone tumors that may be confused with metastatic cancer such as histiocytosis, fibrous dysplasia, and enchondromatosis.[11]

In all cases, appropriate imaging tests are necessary and need to be interpreted in conjunction with the overall clinical picture. Information from the measurement of biochemical markers of bone metabolism (i.e. alkaline phosphatase and calcium) and serum tumor markers may also be helpful.

EVALUATION

The evaluation of bone metastases begins with a detailed history and physical examination. Gradual pain onset indicates mild bone destruction, whereas sudden pain onset, especially in a weight-bearing bone, usually indicates a pathological fracture. The location of the pain is important in determining which diagnostic imaging studies will provide the most useful information. Bone metastases also may produce pain through soft tissue extension. This is most dramatically seen when vertebral body metastases extends extraosseously and compromise the integrity of the spinal canal and spinal cord. Pain is the most common presenting symptom, however, weakness, sensory loss, loss of deep tendon reflexes, and bowel and bladder incontinence may also occur.

Treatment of patients with bone metastases depends on the initial presentation, and an important factor is whether surgery will be included in its management. Certain factors known to be associated with extensive bone loss that would require surgery are included in Table 2. Surgery may be required when a pathological fracture of a long bone has occurred or is at risk of occurring. Neurosurgical intervention may also be required, depending on the clinical and radiographic presentation in patients with spinal cord compromise. In patients undergoing surgical fixation, the marrow cavity of the bone becomes contaminated with neoplastic cells. After the patient has recovered from surgery and the incision has healed, radiation is then delivered to most of the marrow cavity to sterilize the bone of neoplastic cells.

The presence of a solitary bone lesion can present a diagnostic dilemma,

Table 2
Indications for Surgical Fixation in the Management of Bone Metastases

Intramedullary lytic lesions involving 50% or more of the bone's cross-sectional diameter

A lytic lesion involving a length of cortex greater than the cross-sectional diameter of the bone or greater than 2.5 cm in axial length

Pain unrelieved after radiation therapy

Fracture of a weight-bearing bone

Data from Lane et al[20]

since not all patients in pain and with a history of cancer have metastatic disease. Almost one-third of patients may have benign disease with this presentation.[12] A percutaneous needle biopsy is recommended for a first occurrence of metastasis in a solitary bone if it is associated with equivocal imaging studies or is a suspected solitary recurrence after a disease-free interval of greater than two years' duration.

The diagnosis of metastatic cancer to the skeletal system is based on one of several radiographic imaging studies. Plain x-rays of the skeletal system are highly accurate in differentiating metastatic cancer from other benign or malignant lesions of bone. To detect a destructive lesion in trabecular bone on a plain radiograph, it must be greater than 1 cm. in diameter with loss of approximately 50% of the bone mineral content.[13] When bone resorption predominates, focal bone destruction occurs and bone metastasis has a lytic appearance. Conversely, in bone metastasis characterized by increased osteoblastic activity, the lesions appear sclerotic or blastic. There are also mixed lesions seen most commonly in breast cancer which contain both lytic and sclerotic lesions. Lytic lesions are most common in breast, lung, kidney, melanoma, and GI malignancies. Sclerotic metastases are commonly seen in prostate cancer but may also arise from breast, lung, and carcinoid tumors. Plain radiographs also help to define the target volume for radiation, determine the severity of bone destruction, and can help in the decision of whether surgical intervention is required.

Radionuclide imaging of the entire skeletal system is extremely useful in the diagnosis and management of patients with bone metastases. With the development of a reliable bone imaging agent (technicium 99 diphosphate), the gamma camera, and whole body imaging, bone scans have become a routine method for detection, staging, and following the response of abnormal bone lesions to treatment. Bone scans also are used as a guide in performing needle biopsies for solitary lesions. Increased tracer uptake is seen in areas of osteoblastic activity and increased skeletal vascularity with preferential uptake of the tracer at sites of active bone formation. The bone scan accurately reflects the metabolic reaction of bone to the disease process. In general, bone scans will detect metastatic disease months before they are evident on plain x-rays. Bone scans are most sensitive and specific for tumors of the breast, prostate, lung, and kidney. They are least accurate for the diagnosis of multiple myeloma, lymphoma, and leukemias where false negative scans can occur when there is truly lytic disease present. Areas of decreased uptake or photopenic areas are seen with multiple myeloma and occasionally with breast and lung cancers when there has been significant bone destruction with rapidly growing lytic lesions.

> *A substantial percentage of patients with bone metastases may benefit from palliative radiotherapy. Often, this treatment leads to rapid symptomatic improvement with minimal side effects.*

Computed tomography (CT) produces images with excellent soft tissue and contrast resolution and is useful in assessing patients with positive bone scans but negative plain radiographs. In one series of patients with breast carcinoma, 50% had obvious metastasis on CT scan, 25% had benign causes, and in 25%, no abnormality could be detected. None of these patients subsequently developed metastatic disease.[14] CT scan with bone windows may be indicated in certain clinical situations, for example, when evaluating metastases to the base of skull, disease involving the vertebral column or tumors of the pelvis.

Magnetic resonance imaging (MRI) has the advantage over CT of providing multiple planar images which permit evaluation of the entire spine in the sagittal plane. MRI also accurately images the medullary component of bone and is ideally suited for the early detection of metastatic carcinoma, particularly primary infiltrative neoplasm such as leukemia, lymphoma, and multiple myeloma.[15] MRI is able to detect such lesions due to the high signal intensity or brightness of normal marrow, which is mostly fat. With increased cellularity and therefore a higher water content, infiltrating neoplasms will appear as a darker area on T-one weighted images. MRI with gadolinium enhancement of the spine is optimal in evaluating patients with possible spinal cord compromise because it is accurate and, unlike a myelogram, is not invasive. MRI also has been reported to be more sensitive than bone scans for early detection of metastatic disease to the skeleton.[16]

External Beam RT

RT of bone metastasis is undertaken after a thorough assessment of the patient's clinical condition has been completed. This review focuses on external beam RT for palliation of bone metastases; however, the use of systemic radioisotopes, such as Strontium-89, also plays an increasing role in the treatment of selected patients with diffuse bone metastases. When treating the patient with osseous involvement, it is important to understand that significant myelosuppression can be caused by radiation therapy. For this reason, a hematologic profile should always be obtained before initiation of a course of therapy. Factors that should be considered in determining the myelosuppressive effect of radiation therapy include the length of the field chosen and the percentage of bone marrow within the radiated volume. In adults, approximately 15% of the total red marrow is in the skull with 10% in the upper limbs, 40% in vertebral bodies and 25% in lower limbs.[1] The myelosuppressive effect of radiation therapy can be markedly increased if concurrent chemotherapy is delivered.

Generally, radiation treatments are delivered with multifraction regimens. Fractionating treatment spares normal tissues because of cellular repopulation and repair of sublethal damage between dose fractions. At the same time, fractionation increases tumor damage and cell kill because of re-oxygenation and re-assortment of malignant cells.

In practical terms, when treating patients with RT for bone metastases, the goal is to find a dose/fraction scheme that confers a high likelihood of durable pain relief and local tumor control with a minimum of early and late side effects.

In addition, attempts also should be made to minimize the actual number of treatments in the palliative setting. There is significant debate among radiation oncologists about the optimal dose and fractionation schemes for bone metastases. Palliative dose/fraction schemes that have been used have ranged from 800 cGy in a single fraction to 5000 cGy over 25 fractions. A number of groups have investigated various dose-fraction schemes to try to better define optimal regimens. The RTOG Cooperative Study Group assessed pain relief in 759 patients randomized to a variety of dose-fractionation schedules including: 270 cGy x 15 fractions, 300 cGy x 10 fractions, 300 cGy x 5 fractions, 400 cGy x 5 fractions and 500 cGy x 5 fractions. Although no significant differences in degree and time to relief could be detected between the various regimens, an independent re-analysis using the multivariate statistical technique of logistic regression, suggested that the more protracted schedules (270 cGy x 15 fractions and 300 cGy x 10 fractions) were more effective in terms of complete pain relief with subsequent cessation of narcotic analgesics.[17]

In another study undertaken at the Royal Marsden Hospital in England, researchers randomized 288 patients with symptomatic bony metastasis to receive 800 cGy in a single fraction versus 300 cGy for 10 daily fractions.[18] The patients were well balanced in terms of tumor type. Pain relief was subsequently assessed with a questionnaire completed by patients at home. There was no difference in the percentage of patients responding to treatment (80%) or in the duration of pain relief or durability of response. In the single fraction group, however, a larger number of patients were subsequently treated with re-irradiation to the same site. Of interest, pain relief was independent of the histology of the primary tumor. No late complications were reported in the single fraction group.

In clinical practice, the decision to deliver a short course of large fraction RT versus a more protracted course of therapy is usually based on multiple factors. These should include the patient's prognosis and performance status, as well as the anatomic site of treatment. Although some sites may be amenable to a very short course of therapy with few acute side effects (e.g. femur), other sites such as the abdomen do not tolerate large fractions sizes well. In addition, in patients who may survive many months or years, there remains a concern that large fraction size may produce significant late effects in certain tissues, such as the brain and spinal cord.

In an attempt to minimize the number of visits for RT in patients with widely disseminated bone metastases, a few groups have explored the use of sequential hemibody RT. Although treatment is usually done with a single fraction of 600 to 800 cGy, a short hospitalization is necessary with pre-medication for nausea and IV hydration. In an RTOG study assessing the value of hemibody RT, complete pain relief was reported in 21% of patients and partial relief in 77% of patients.[19] Pain control was achieved quickly with 80% of responding patients seeing improvement within one week. This treatment is not without morbidity, however, with severe or life threatening nausea/vomiting, diarrhea or hematologic toxicity seen in 2 to 8% of patients treated to the lower or mid- body. In patients treated to the upper body, who had previously received intensive chemotherapy, the severe toxicity rates were even higher.

SUMMARY

Bone metastases are a common problem in patients with cancer and frequently result in significant pain and functional disability. An understanding of the pathogenesis of metastatic bone involvement and appropriate diagnostic evaluation often leads to earlier institution of palliative therapy. A substantial percentage of patients with bone metastases may benefit from palliative radiotherapy. Often, this treatment leads to rapid symptomatic improvement with minimal side effects.

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Rhode Island Cancer Pain Initiative and Its Role in Physician Education

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It has been estimated that at least two-thirds of cancer patients with advanced disease will experience pain during the course of their illness.[1] As techniques for control of cancer pain are available in the United States, one wonders why this is the case and how this situation might be remedied.

Many barriers currently exist which impede the efficient and efficacious management of pain in patients with cancer.[1] These include deficits in the education of health care professionals in the area of pain management, cultural and social barriers to the proper use of opioids in chronic pain, some of which is exacerbated by the government's "just say no to drugs" campaign, and legislative and legal barriers to effective prescribing of opioids such as duplicate prescription forms. Other barriers include misinformation on the part of patients and families, and fears related to the "meaning of pain" that interfere with clear communication between patients and their health care providers. The outpouring of information in medial journals, books, and conferences over the last decade and the introduction of the AHCPR Cancer Pain Guidelines in March 1994 has not completely remedied this situation, but are steps forward in the fight against cancer pain.

One additional ally in the battle to further the state of the art of cancer pain management has been the inception of state cancer pain initiatives. In December 1986, 65 Wisconsin health professionals and representatives from state regulatory agencies held a statewide strategy session to determine how pain management might be improved. Their efforts evolved into the Wisconsin Cancer Pain Initiative. The World Health Organization then designated the Wisconsin Cancer Pain Initiative a demonstration site in its worldwide effort to alleviate the suffering of cancer patients in pain. This effort has blossomed; currently every state has or is forming a state cancer pain initiative. (Figure 1)

Abbreviations Used

AHPCPR	Agency for Health Care Policy and Research
CPM	Cancer Pain Management
ECOG	Eastern Cooperative Oncology Group
RICPI	Rhode Island Cancer Pain Initiative
STATVIEW	Macintosh statistical program

Founded in June 1991, the Rhode Island Cancer Pain Initiative (RICPI) is a nonprofit volunteer interdisciplinary organization open to physicians, nurses, pharmacists, social workers, clergy, psychologists, physical, occupational and recreational therapists, regulators, and patients and their families. RICPI is fortunate in having had, since its inception, the strong support of the Rhode Island Division of the American Cancer Society.

The goals set forth by RICPI are:

1) Improving pain management knowledge, skills, and attitudes among health care professionals,
2) Promoting knowledge about cancer pain relief among patients, families, and the general public,
3) Identifying common barriers to adequate cancer pain relief and finding solutions,
4) Acting as a liaison with other organizations,
5) Developing and disseminating information about cancer pain relief, and,
6) Promoting the research and evaluation of cancer pain management.

To achieve these goals, RICPI initially established subcommittees devoted to research and evaluation, physical, pharmacist and nurse education, legislative and legal issues, holistic alternatives, and consumer issues and education.

PHYSICIAN EDUCATION

The attitudes of physicians and physicians-in-training, coupled with factual knowledge deficits, have been noted to be major obstacles to appropriate pain relief.[2,3,4] The Wisconsin Cancer Pain Initiative has hypothesized that cancer pain relief is a low priority for physicians because the consequences of inadequate pain relief are not well appreciated; there is a lack of consensus as to what constitutes good pain management; and, there has been a lack of consistent incentives for appropriate pain management such as the threat of malpractice or quality assurance criteria[3]

Factual knowledge deficits have been noted in the following areas: exaggerated incidence of addiction and fallacy that increasing pain was invariably related to the development of drug tolerance, rather than progression of the underlying disease. These were compounded by a lack of knowledge of newer methods of pain management and the basic principles of analgesic therapy, including site of action, duration, bioavailability, toxicity, and potential drug interactions, and a lack of understanding of cancer pain pathophysiology.[4]

Physicians are the reflection of the attitudes of the society from which they come, coupled with the expectations for cure of disease with which that society endows them. They are often held responsible for the cure of the patient in whom "no sophisticated medical or surgical intervention will significantly alter the course of the disease, and the patient serves as a constant reminder of human frailty and the impotence of modern medicine."[5] The most recent study on physician attitudes and practices by Von Roenn further corroborates that 86% of physicians in ECOG-affiliated institutions responding to the survey felt that the majority of cancer patients' pain was untreatable.[6] They felt that analgesic prescribing was limited secondary to concerns about side effect management and tolerance, and the majority of physicians (76%) thought poor pain assessment was the single most important barrier to effective pain management. Of the 900 respondents, 88% felt that medical training in cancer pain management was less than good, and 73% that residency training in this area was less than good.

To address these issues on a local level, a resident survey was developed to help the Rhode Island Cancer Pain Initiative Physician Education Committee adapt the current teaching approach to the concerns of local house officers in internal medicine and family practice. The data from this survey is presented here.

METHODS

Anonymous surveys were distributed to house officers attending noon conferences at the five Brown University affiliated programs in internal medicine and family practice. House officers who attend these conferences care for patients on the ward that month. The chief residents at each of the participating hospitals distributed and collected surveys from house officers at noon conferences.

Questions were asked concerning previous exposure to information on cancer pain management during medical school and residency, awareness of cancer pain initiatives, personal familiarity with cancer pain management, personal comfort managing cancer pain, the residents' opinions concerning what has most influenced their present management of cancer pain, where they would like to see more formal training, and whether they believe cancer pain can be relieved. Basic frequencies were computed using STATVIEW, and contingency tables were computed with significance levels set at p<.05.

RESULTS

Table 1 illustrates the survey responses of 74 internal medicine and family practice residents, constituting a convenience sample of the approximately one-third of residents on wards at any given time. The sample was predominantly (81.1%) individuals trained at US medical schools.

Of those who received instruction in cancer pain management during the medical school clerkships, 31 (41.9%), it was most often provided during medicine, 29 (39.2%). Forty-nine (66%) of residents in the sample had received some clinical instruction from an attending, and only 20 (27%) of the sample remembered instruction from one of their residents.

Residents had variable exposure to information on this topic during medical school and residency. Residents indicated more instruction from their clinical attendings than from any other sources during medical school or residency. Overwhelmingly, 71 (95.9%) of the residents felt that cancer pain could be relieved; however, the majority, 47 (63.5%) of the residents did not feel comfortable managing cancer pain. In addition, the majority of residents, 60 (81%) would like to see more training in cancer pain management at the residency level.

> *Over the past three years, individual seminars on cancer pain management were presented at each of the Brown University affiliated residency programs in medicine and family medicine.*

Thirty-four (56.7%) of the medical residents and 13 (92.9%) of the family practice residents did not feel comfortable managing cancer pain. Eighteen (78.3) of those who felt comfortable managing cancer pain had a formal lecture on the subject in medical school. Thirty-one (66%) of those who were not comfortable managing cancer pain had not had a lecture.

Those who had clinical instruction from an attending were more evenly divided on the question of whether they felt comfortable. Twenty (40.8%) felt comfortable and 26 (53.1%) did not feel comfortable managing cancer pain. Of those who did not have attending level instruction, however, 21 (84%) did not feel comfortable managing cancer pain.

DISCUSSION

In its first year of operation, RICPI's physician education committee set as its goal the provision of educational seminars to physicians at all levels of training. This was accomplished by developing individual seminar formats appropriate to the setting in which it was to be delivered. In the first year Brown Medical School course on biopsychosocial aspects of medicine and the development of interviewing skills, a module was presented by a physician-nurse team on the assessment and interview of the patient in pain. In the fourth year elective in clinical pharmacology, an interdisciplinary team, composed of a physician, nurse, and clinical pharmacologist, presented a combination didactic/case discussion module.

The challenge for the committee was to identify ways in which knowledge could be imparted to help residents feel more comfortable managing this problem, with the hope of ultimately positively affecting the patient experience. Over the past three years, individual seminars on cancer pain management were presented at each of the Brown University affiliated residency programs in medicine and family practice, as well as at the local Veterans Administration Hospital, which is staffed by the local residency programs. Once again, an interdisciplinary team made the presentation to residents to emphasize that pain is most effectively managed through a team approach. It was hoped that this approach would break the stereotype that physicians can only learn from physicians. The physician presented a didactic lecture on the prevalence of cancer pain, its assessment and treatment. The nurse made the case presentation. The full team was available for questions and answers at the conclusion of the session. In addition, at each hospital on-site "resources" were introduced, whom the residents could contact with further questions and problems. At each conference presented, assorted educational materials were made available to the residents detailing the World Health Organization's step ladder approach to pain management and drug equivalencies. Most of the participating residency programs have recognized the importance of this information and have proceeded to provide conferences on this topic on their own. Other formats were presented at the attending level as well.

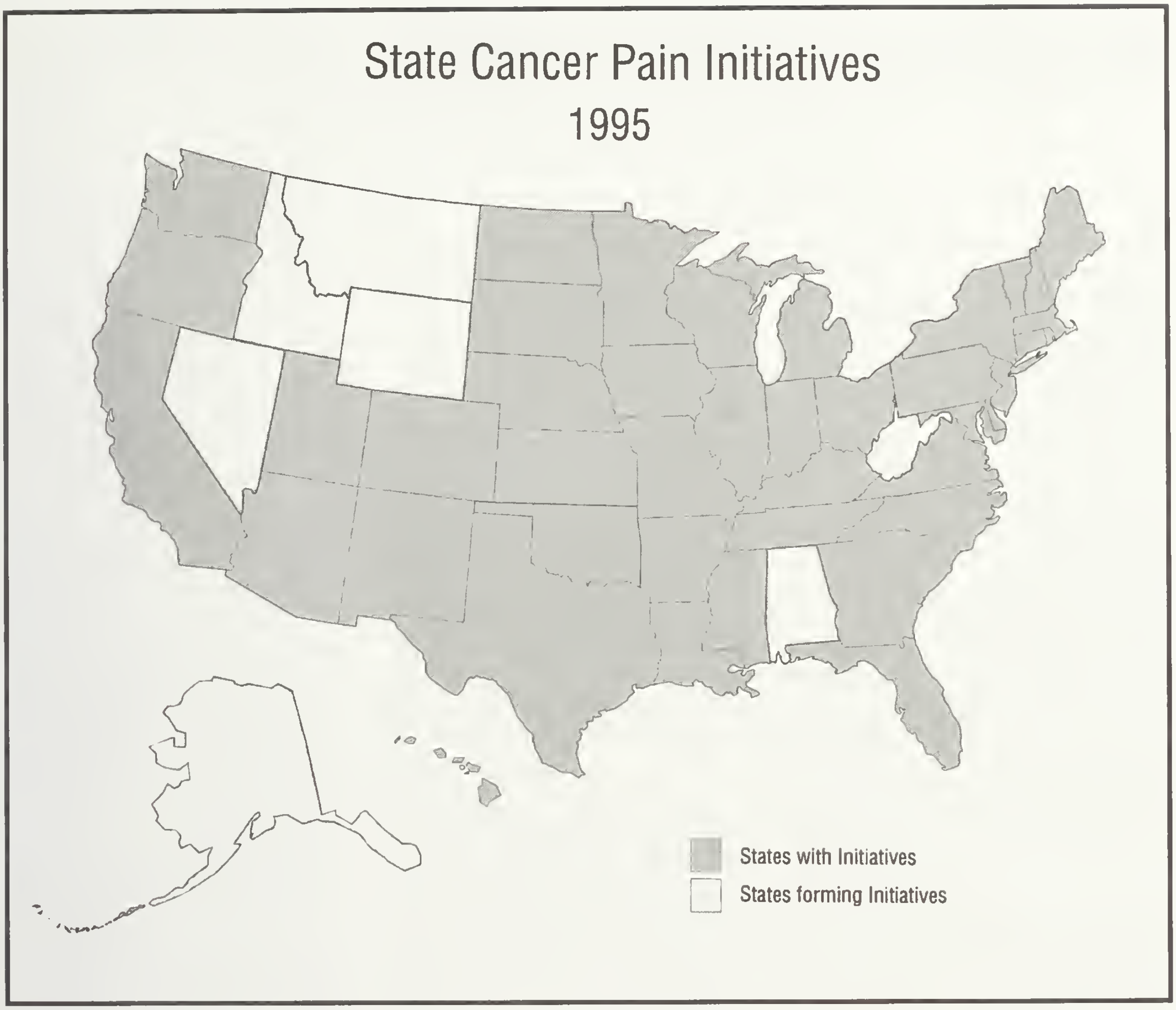

Figure 1. Courtesy of the National Cancer Pain Initiatives Resource Center, December 1995.

The most encouraging aspect of this survey was the finding that of the medical and family practice residents in a university-wide program, 96% felt that cancer pain could be relieved; however, 64% admitted to not feeling comfortable managing the problem.

Having identified prevailing concerns and attitudes through a convenience sample of medicine and family practice house staff, the issue is how to provide appropriate information to help residents feel more comfortable managing cancer pain. RIPCI has developed on model for educating physicians based on available resources. The Wisconsin Initiative, a leader in this area, created a mutlimodality effort designed to increase factual knowledge, legitimize the importance of pain assessment and treatment, and emphasize the importance of role modeling in the learning process.[3] The management of cancer pain needs to be made as high a priority as other areas of clinical practice. "In particular, attending physicians can serve to impart the humane attributes of medical practice to their students ... While most student physicians can recall an experience whereby an attending physician took them to task for prescribing the wrong antibiotic or failing to properly evaluate fever in the neutropenic patient, few can probably recall being similarly chastised for poorly controlling a patient's pain."[3] The difficulty lies in the fact that few, if any, attending-level physicians ever received specific training in the art and science of cancer pain management during their own clinical training.

It also has been suggested that all physicians, regardless of specialty, need to take responsibility for the assessment and treatment of pain. This avoids the potential trap of individual subspecialists treating specific disease entities and symptom complexes, or almost as sadly, for total abdication of responsibility for pain management to a specialized pain team, if one exists. The Wisconsin Initiative astutely pointed out that primary care physicians continue to act as primary caregivers for most cancer patients in Wisconsin, and therefore, have directed much of their effort toward these physicians.[2]

These efforts have consisted not only of careful assessment of prevailing knowledge and attitudes and the dissemination of current knowledge, but also the use of role modeling techniques to improve knowledge and overcome inappropriate attitudes. MB Max agreed with this approach emphasizing that "educational efforts must, however, interface with practitioners on the wards; behavior change is more effective when intervention occurs as close as possible to the site and time of action, includes prompt feedback in cases of ineffective prescribing, and involves respected peers as role models."[7]

The publication in March 1994 of the AHCPR Guidelines for the Management of Cancer Pain set the stage for improving current educational efforts. It is incumbent upon the current generation of physicians to take responsibility for enlarging its own knowledge base is this area and to assume the burden of serving as role models for those following their footsteps. Only, by doing so, may it be possible to reverse the dreadful, needless suffering of the cancer patient in pain.

Table 1
Frequencies

Residency year	PGY-1 32 (43.2%) PGY-3 26 (35.1%)	PGY-2 15 (20.3%) PGY-4 1 (1.4%)
Residency type	Medicine 60 (81.1%) Family Practice 14 (18.9%)	
Aware of cancer pain initiative	US 60 (81.1%)	Foreign 12 (16.2%)
Assigned reading on cancer pain management in medical school	25 (33.8%)	
Received medical school lecture on cancer pain management	37 (50%)	
Received clerkship instruction in cancer pain management in medical school	31 (49%) Medicine 29 (39.2%) Surgery 5 (6.8%) Other 5 (6.8%) OB/GYN 2 (2.7%) Community Health 2 (2.7%) Pediatrics 1 (1.4%)	
Received instruction from attending	During clinical training 49 (66.2%) From resident 20 (27.0%) From intern 7 (9.5%) From medical student 1 (1.4%)	
What has most influenced resident's current management of cancer pain	Ward experience 41 (55.4%) Personal familiarity 9 (12.2%) Multiple answers 9 (12.2%) No response 8 (10.8%) Clinical teaching 6 (8.1%) Didactic teaching 1 (1.1%)	
Would like to see more formal training at level of	House officer 60 (81.1%) Medical school 27 (36.5%) Journals 16 (21.6%) CME Courses 8 (10.8%)	
Feel comfortable managing cancer pain	Yes 23 (31.1%)	No 47 (63.5%)
Have personal familiarity (family, friend) with cancer pain management	Yes 22 (29.7%)	
Think cancer pain can be relieved	Yes 71 (95.9%)	No 1 (1.4%)

Resources

RI Cancer Pain Initiative (401) 722-8480, 1-800-227-2345
AHCPR Cancer Pain Guidelines 1-800-4-CANCER

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Regulatory Issues Relating to the Management of Patients with Cancer Pain and Pain of Non-malignant Origin

Milton W. Hamolsky, MD, Bruce W. McIntyre, Esq., Nikki Deary, and Norman Phelps

The Rhode Island Department of Health (Department) is sensitive to the difficulties encountered by health care providers in the treatment of patients with cancer pain and pain of non-malignant origin. Many providers have expressed discomfort with the perceived negative effect of statutory and regulatory requirements on their ability to manage the pain of their patients. Such concerns are relevant to the Department of Health's regulatory oversight activities of the Board of Medical Licensure and Discipline, which licenses and disciplines physicians, and the Division of Drug Control, which regulates the manufacture, distribution, prescription, administration, and dispensing of controlled substances. It is the hope of the Department that this article will alleviates some concerns and broaden the understanding of its licensees regarding the management of intractable pain.

BOARD OF MEDICAL LICENSURE AND DISCIPLINE

The Rhode Island Board of Medical Licensure and Discipline (Board) continues to see cases in which serious problems in the management of long-term intractable pain are encountered by patients and physicians. The Board is aware of the perception that many physicians "under-treat" such patients based on a fear of "causing addiction;" on the other hand, it receives many allegations of the improper, sometimes illegal, "over-use" of controlled substances, which are regulated by state and federal law. Given that pain management is a national problem, the Board undertook a review of guidelines adopted by various state medical boards (Colorado, Texas, New Jersey, Massachusetts, and California) concerning the appropriate management of patients with long-term intractable pain. We were most impressed with the guidelines developed by the State of California.

The California guidelines resulted from a state-sponsored conference in which 120 health care practitioners, educators, representatives from professional schools and associations, and health care consumers met to recommend solutions to legal, professional, and educational barriers to effective pain management. The Governor of California, issued a report, *Summit on Effective Pain Management: Removing Impediments to Appropriate Prescribing*, on the conference, which was reviewed by the Rhode Island Board of Medical Licensure and Decision. This review was part of the Board's decision to adopt the following guidelines to help the practicing physician to deal with this difficult problem.

GUIDELINES FOR LONG-TERM PAIN MANAGEMENT

ADOPTED ON JUNE 14, 1995

1. History/Physical Examination

A medical history and physical examination must be accomplished. This includes an assessment of the pain, physical and psychological function, substance abuse history, assessment of underlying or coexisting diseases or conditions, and should also include the presence of a recognized medical indication for the use of a controlled substance.

2. Treatment Plan, Objectives

The treatment plan should state objectives by which treatment success can be evaluated, such as pain relief and/or improved physical and psychosocial function, and indicate if any further diagnostic evaluations or other treatments are planned. The physician should tailor drug therapy to the individual medical needs of each patient. Several treatment modalities or a rehabilitation program may be necessary if the pain has differing etiologies or is associated with physical and psychosocial development.

3. Informed Consent

The physician should discuss the risks and benefits of the use of controlled substances with the patient, guardian or authorized representative. This discussion should be documented and signed by the patient, guardian or authorized representative.

4. Periodic Review

The physician should periodically review the course of opioid treatment of the patient and any new information about the etiology of the pain. Continuation or modification of opioid therapy depends on the physician's evaluation of progress toward treatment objectives. If the patient has not improved, the physician should assess the appropriateness of continued opioid treatment or trial of other modalities.

5. Consultation

The physician should be willing to refer the patient as necessary for additional evaluation and treatment in order to achieve treatment objectives. In addition, physicians should give special attention to those pain patients who are at risk for misusing their medications including those whose living arrangements pose a risk for medication misuse or diversion. The management of pain in patients with a history of substance abuse requires extra care, monitoring, documentation, and consultation with addiction medication specialists, and may entail the use of agreements between the provider and the patient that specify the rules for medication use and consequences for misuse.

6. Records

The physician should keep accurate and complete records according to items 1-5 above, including the medical history and physical examination, other evaluations and consultations, treatment plan objectives, informed consent, treatments, medications, agreements with the patient, and periodic reviews.

7. Compliance with Controlled Substance Laws and Regulations

To prescribe controlled substances, the physician must be licensed appropriately in Rhode Island, have a valid controlled substances registration and comply with federal and state regulations for issuing controlled prescriptions. Physicians are referred to the Physicians Manual of the US Drug Enforcement Administration and the General Laws of Rhode Island relating to the Board of Medical Licensure and Discipline and the Division of Drug Control of the Rhode Island Department of Health.

DIVISION OF DRUG CONTROL

On May 12, 1978, the Rhode Island Legislature passed Title 21, Chapter 28, Uniform Controlled Substances Act, which is enforced by the Department of Health, Division of Drug Control. This act delineates the standards and schedules of controlled substances as well as the regulation of the manufacture, distribution, prescribing, administration, and dispensing of controlled substances. At the time of its original passage, section 21-28-3.18 (i) reflected the following:

> *"(i) Prescriptions for controlled substances as found in schedules II, III, and IV of section 21-28-2.08 will become void unless dispensed within seven (7) days of the original date of the prescription. Said prescriptions cannot be written for more than one hundred (100) dosage units and not more than one hundred (100) dosage units may be dispensed at one time."*

In response to the needs of its provider population, on July 20, 1993, a legislative amendment to this section was passed, spearheaded by the Department of Health, which increased the maximum dosage units that may be prescribed for Schedule II controlled substances. The amended section now reads as follows:

> *" (i) Prescriptions for controlled substances as found in schedules II, III, and IV of section 21-28-2.08 will become void unless dispensed within seven (7) days of the original date of the prescription. Said prescriptions in schedules III and IV cannot be written for more than one hundred (100) dosage units and not more than one hundred (100) units may be dispensed at one time."*

The Department of Health intends to continue its efforts to work with the physician community to assure that patients receive the most appropriate treatment for the effective management of long-term pain.

> *"(j) Prescriptions for controlled substances as found in schedule II may be written for up to a 30-day supply, with a maximum of two hundred and fifty (250) dosage units, as determined by the prescriber's directions for use of the medication. In no event shall more than a 30-day's supply, up to a maximum of two hundred and fifty (250) dosage units, be dispensed at one time."*

It has been demonstrated that these amendments have facilitated the management of long-term pain. The Department, however, recognizes the continuing burden imposed upon physicians to comply with the regulatory requirements for the use of the duplicate prescription forms for schedule II drugs. The Department of Health continues to advocate the elimination of the duplication prescription program in Rhode Island. It is hoped that funding can be obtained to implement an Electronic Data Transfer Program authorized by the Uniformed Controlled Substances Act. This program will negate the necessity for the two-part prescription now in use.

The Department believes that the actions taken by the Rhode Island Board of Medical Licensure and Discipline to disseminate the "Guidelines for Long-Term Pain Management" and the Department's successful efforts to amend the Controlled Substances Act will facilitate the appropriate prescription and use of controlled substances in the treatment of patients with long-term pain. Further, when resources permit, the Department intends to implement a computerized process for monitoring the use of controlled substances that will facilitate the prescribing of these substances by clinicians, while providing more useful monitoring information to the Division of Drug Control. The Department intends to continue its efforts to work with the physician community to assure that patients receive the most appropriate treatment for the effective management of long-term pain.

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The Costs of Unrelieved Pain

Wendy M. Stein, MA, NHA, MD

There were 1.2 million Americans diagnosed with cancer during 1992; 526,000 were estimated to have died from cancer in 1993, of which as many as 70% were expected to die of unrelieved pain.[1] Clearly, cancer and specifically cancer pain are significant problems. Although cancer pain is used as a model in this paper because it has been better studied than many other types of pain, much of what is discussed is directly applicable to most types of chronic pain.

"Cost" is defined by Webster's Dictionary as "the loss or penalty incurred in gaining something." In unrelieved pain, there is nothing to be gained, and a considerable price is paid not just by the patient, but by the patient's family, health care professionals, and society at large.

COSTS TO THE PATIENT

Untreated or unrelieved pain has been implicated in increased psychiatric comorbidity, altered immune function, impaired function, diminished quality of life, loss of autonomy, and suffering.[2,3] Studies have shown an increased frequency of psychiatric disorders found among cancer patients with pain, particularly adjustment of disorder with depressed or anxious mood, and major depression.[2] Approximately 25% of all cancer patients experience severe depressive symptoms with a prevalence that increases to 77% among those with advanced illness.[2] "The recognition and treatment of depression can be considered as an effort to restore authentic autonomy, allowing the patient the ability to consider carefully, correlate, and communicate his/her wishes and goals."[4]

ABBREVIATIONS USED

AHCPR	Agency for Health Care Policy and Research
AIDS	Acquired immune deficiency syndrome
NK	Natural killer (cell)

Uncontrolled pain also has been cited as a major factor in cancer suicide. Although relatively few cancer patients take their own lives, when compared with studies of other diseases such as AIDS, cancer patients are known to be at increased risk. In a 1985 study by Levin and Cleeland, the fear of unacceptable pain accounted for a major component of requests to physicians for assisted death and was so important to patients with cancer that 69% reported that they would consider committing suicide if their pain was not adequately managed.[2]

The interactions between the central nervous and endocrine systems, and immune functions are just beginning to be understood. Pain has been implicated in alterations in immune function. Page et al conducted a study on rats using a mammary adenocarcinoma sensitive to natural killer cell activity (NK).[3] NK activity has been found to be particularly important in controlling tumor growth, especially metastatic growth. Their research showed that surgery enhanced metastatic colonization, and this tumor-enhancing effect occurred only during the time in which the tumor was sensitive to NK control. They found that an analgesic dose of morphine blocked the surgery-induced increase in metastasis. Their findings suggest that uncontrolled postoperative pain was a critical factor in promoting metastatic spread.[3]

It is well accepted that pain is both subjective and multidimensional.[5,6,7] Rene Leriche defined physical pain as ". . . not a simple affair of an impulse traveling at a fixed rate along a nerve. It is the resultant conflict between a stimulus and the whole individual."[8] Pain has physical (symptoms), functional (task performance), emotional (mood), social (perceived social support, maintenance of leisure activities, family and community functioning, intimacy, sexuality), and spiritual dimensions.[6] All of these have to be addressed to successfully relieve total pain.

Commonly studied areas of health services research have included the effect of health care services on longevity, symptoms, physiologic abnormalities, satisfaction, function, psychosocial factors, and compliance. "Functional status, quality of life, and utility measures have developed out of a need to define to a greater extent the effects of health care interventions and the impact of disease on the individual as well as groups of individuals with chronic disease."[9] Quality of life studies, in particular, have generated substantial attention.

Quality of life has been defined in many ways. Clinch and Schipper in the *Oxford Textbook of Palliative Care Medicine* included physical concerns, functional ability, family well-being, spirituality, social functioning, treatment satisfaction including financial concerns, future orientation, sexuality, and intimacy, and occupational functioning.in their definition of the dimension of quality of life.[10] The multifactorial nature of pain naturally lends itself to quality of life research as defined above. It is easy to see why the World Health Organization stated that " nothing would have a more immediate effect on quality of life and relief from suffering, not only for the cancer patients, but also for their families, than implementing the knowledge accumulated in the field of palliative care."[11]

Feelings of loss of control and suffering can be just as devastating as physical pain itself. Suffering was defined in the AHCPR guidelines as "the state of severe distress associated with events that threaten the intactness of the person . . .The suffering of patients with terminal cancer can often be relieved by demonstrating that their pain truly can be controlled.[12] Appropriate pain management can restore to an individual some of the control wrested from him by the disease.[13]

COSTS TO FAMILIES

It has been estimated that two-thirds of American families have at least one family member diagnosed with cancer.[6] Since approximately 75% of patients will experience pain at some point during the course of their disease, a significant number of family members will be affected by cancer pain.

Dr. Betty Ferrell and colleagues at the City of Hope National Medical Center have spent considerable time studying the effects of cancer pain on family members.[6,7,8,14,15] In one study of 85 caregivers of cancer patients with pain, 72% of the caregivers were women with a mean age of 54 years. Family members characterized their relatives' pain with descriptors suggestive of anatomic and hidden pain, family fear and suffering, and overwhelming/unendurable pain. The three major themes that emerged from this study were helplessness, coping by denying feelings and wish for death.[7]

Clearly, the suffering of the patient in pain is not his or hers to bear alone.

COSTS TO HEALTH CARE PROFESSIONALS

The goal of medicine is the eradication of disease. Beyond that goal, medicine should seek to:

- relieve symptoms, pain and suffering
- improve functional status or maintain compromised status
- educate and counsel patients regarding their condition and its prognosis
- prevent untimely death, and
- promote health and prevention of disease.[4]

Health care professionals recognize how frustrating this role can be. In a study by Solomon, 81% of physicians and nurses feel that the most common form of narcotic abuse in the care of the dying is the undertreatment of pain.[4] Although most of the medications and techniques for effective pain management have been available for many decades, the majority of nurses and physicians currently in practice never received formal training specifically in the area of pain management. Inability to adequately manage pain leads to feelings of helplessness and inadequacy on the part of the health care providers.

COSTS TO SOCIETY

Unrelieved or inappropriately treated pain is costly to society. Invasive, more expensive routes of administration of medication that are constant reminders of disease are often used because they are reimbursed by insurance carriers, when simpler, less invasive routes that provide greater patient autonomy are not. Patient-controlled analgesia, a wonderful tool developed to treat postoperative pain on a short term basis, has been estimated to cost as much as $4,000 a month, amounting to almost $50,000 a year in the case of a cancer patient with chronic pain.[16] This price is just part of an individual's care.

There are an estimated 34 million people without health insurance, and 80 million who are underinsured in the face of major illness. Many of these individuals whose pain might be adequately controlled at home with appropriate pain management are emergently admitted to acute care hospitals at a significant cost to the health care system.

> *In a recent study, 81% of physicians and nurses felt that the most common form of narcotic abuse in the care of the dying is the undertreatment of pain.*

* * *

City of Hope National Medical Center looked at the cost of hospital admissions for unrelieved pain. They reviewed 5,772 admissions between November 1989 and October 1990, of which 2,795 were scheduled admissions and 2,977 were unscheduled. Two hundred fifty-five unscheduled admissions (approximately 4%) had a primary admitting diagnosis of uncontrolled pain; of these, 26% had at least one previous admission for uncontrolled pain, and 54% of these occurred within two weeks of the hospital discharge. The average length of stay of this group was 12 days, at a conservative cost estimate of $20,000 based on an average daily hospital cost of $1,771. These admissions for unrelieved pain amounted to a cost of $5.1 million over a one year period for this one institution. The potential for cost savings in both dollars and human suffering is tremendous.

There are indirect costs to the health care system as well in terms of litigation. "The law is the mechanism by which society translates its values and goals into substantive rules and resolves disputes."[17] Patients and their families have a right to expect adequate pain and symptom management as part of their health care. A landmark case in this regard was that of *The Estate of Henry James v. Hillhaven Corporation*, in which a jury found in favor of the plaintiff in the amount of $15 million for compensatory and punitive damages for inadequate pain management.[18] The patient, Mr. James, was a 75-year-old man with stage III prostate carcinoma. He was hospitalized from December 1986 to January 31, 1987 where his pain was effectively managed on a fixed dose of concentrated oral morphine solution, every three to four hours, around the clock. When he went home, his family continued this regimen with similar success. On February 2, 1987 he was transferred to a nursing home. His physician stated that the patient's prognosis was poor and that the goal of the care was relief of the pain, and continued his previous opiate order. The director of nursing felt that the patient was "addicted" to morphine and instituted an alternate plan without physician approval, which consisted of delaying or withholding the narcotic and giving the patient mild tranquilizer. For 23 days, until he was discharged on February 24 1987, he did not receive pain medication as ordered, resulting in uncontrolled severe pain.[17]

Unrelieved pain results in considerable anguish and suffering for patients, their families, and those who care for them. Additionally, unrelieved pain is an added financial drain on an already overburdened health care system. The "price" of unrelieved pain is one we can no longer afford to pay.

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Of Rodents, Humankind, and Cholesterol

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An article by Drs. Newman and Hulley in the January 3rd issue of the *Journal of the American Medical Association* (JAMA) raised concerns regarding the carcinogenicity of almost all classes of lipid-lowering drugs with the exception of niacin and probucol.[1] Renewed concerns were prompted by a reevaluation of rodent carcinogenicity studies for hypolipidemic drugs. These data were originally provided by pharmaceutical companies, published in the 1992 and 1994 versions of the *Physicians' Desk Reference* (PDR), and abstracted by the authors. A critique of this article by Drs. Dalen and Dalton appeared in the same issue of JAMA.[2] Because of widespread interest in this topic, related articles subsequently appeared in the lay press, and at least one drug company publicly refuted the conclusions of Newman and Hulley.

Data from the second National Health and Nutrition Examination Study indicated that 30% of adults in the US have borderline high cholesterol levels, and 27% have high levels. Data from the 1993 Behavioral Risk Factor Survey for Rhode Island indicated that 29% of adults had not had their cholesterol checked within the past five years. Given the widespread use of hypolipidemic drugs for the prevention of coronary heart disease (CHD), the potential for even more widespread use of these drugs with better adherence to cholesterol screening guidelines, and the fact that patients, particularly those who are asymptomatic, may be treated with these drugs for decades, a review of these findings is indicated.[1] This article evaluates statements made in defense of cholesterol-lowering drugs, the statins in particular, with respect to the two JAMA articles.

ABBREVIATIONS USED

AUC	Area under the curve
CAD	Coronary artery disease
CHD	Coronary heart disease
HMG-CoA	3-hydroxy-3-methylglutaryl coenzyme A
JAMA	Journal of the American Medical Association
PDR	Physicians' Desk Reference
RR	Relative risk

The risk of cardiac morbidity/mortality among hypercholesterolemic patients is high.

It has been established that the relationship between total serum cholesterol and the risk of CHD appears to be continuous and graded. Neither Newman and Hulley nor Dalen and Dalton minimize the risks of CHD in patients with hypercholesterolemia. Newman and Hulley state that it is reasonable to treat high blood cholesterol with cholesterol-lowering drugs in patients with coronary or other atherosclerotic disease. They cite the Scandinavian Simvastatin Survival Study, conducted with patients with known CHD, which strongly suggests that the benefits of cholesterol lowering in men exceed the risks in the short term (5 years), and they cite meta-analyses of other classes of cholesterol-lowering drugs which likewise suggest a mortality benefit in patients at high short-term risk of CHD.[3] Furthermore, they cite minutes of the Food and Drug Administration's Endocrinologic and Metabolic Drugs Advisory Committee meetings at which the decision was made to approve the relabeling of gemfibrozil for prevention of CHD, although only for the "narrow group of patients in whom the Helsinki Heart Study suggested the greatest likelihood of benefit – [Type IIb] patients with low HDL-C, elevated LDL-C, and triglycerides *who have had an inadequate response to weight loss, diet, exercise, and other pharmacologic agents such as bile acid sequestrants and nicotinic acid.*"[1] [Italics ours]

Dalen and Dalton echo the benefits of lowering cholesterol in high risk patients. They expand these recommendations to a larger group that includes asymptomatic persons with coronary artery disease (CAD). They note that patients with CAD are asymptomatic until they have advanced disease, and that the first clinical evidence of disease for at least 20% of persons with CAD is sudden cardiac death, which accounts for half of all CAD mortality. These observations are used to make a case for primary prevention of CAD by lowering elevated cholesterol levels based on safety considerations. The authors note, however, that cost-effectiveness studies of hypolipidemic drugs for the purpose of preventing CHD death or total mortality argues against use of these drugs, particularly when they are used for primary prevention. If the costs of treating patients with angina pectoris and myocardial infarction are factored into these studies, a better case is made for use of cholesterol-lowering drugs for primary prevention of CAD. They conclude that it is "appropriate to reassess the age at which it is proper to begin drug therapy to lower cholesterol levels in asymptomatic patients," hence allowing for treatment based on factors (e.g., cost effectiveness) in addition to safety considerations alone.

Newman and Hulley's article is not based on new information.

The article is not based on new information, but is based on newer methods for calculating systemic drug exposure which more accurately represent cellular exposure and reflect the risk for carcinogenicity. Prior to 1994, relative exposures (the ratio of animal/ human exposures) were presented in terms of milligrams per kilogram (mg/ kg) of body weight. Recognition of the differences in drug absorption, metabolism, and excretion between species prompted a change to relative exposures based on drug blood levels over time (mean drug blood level or the area under the curve, "AUC," when drug blood levels are plotted against time). When the newer exposure measures are used, relative exposures at which carcinogenesis occurs decrease. For example, in one study the carcinogenic dose for lovastatin in mice was 312 times the maximum recommended human dose when exposures were measured in mg/ kg, but this fell sharply to 3-4 times the maximum recommended human dose when AUC measurements were used.

In the referenced studies, rodents were given dosages of lipid-lowering drugs many times the maximum recommended dose for humans.

This is true if one uses the older standard of relative exposures. However, the FDA has changed its policy regarding the best way to express dose equivalency, the more recent PDRs reflect this change, and efforts are underway to use drug blood levels to standardize international drug testing requirements. Hence, it appears that newer measures of exposure and relative exposure will continue to be used and their use will become more widespread.

By the authors' own admission, extrapolation of evidence of carcinogenesis from rodents to humans is a controversial and uncertain process at best.

This is true, and acknowledged by Newman and Hulley, but it is the standard by which all drugs are evaluated. Therefore, this argument cannot be used to question the findings of Newman and Hulley alone, but must be used to question the applicability of all rodent carcinogenicity studies to humans. Authors of both articles point out that mechanisms of carcinogenesis in rodents and humans may be dissimilar, particularly with respect to hepatic carcinogenesis. This is because hepatic carcinogenesis is associated with striking peroxisomal proliferation in rodents but not in humans. Of the 26 rodent carcinogenicity studies cited in the 1994 PDR and reviewed by Newman and Hulley, however, neoplasia was observed in twenty, and of those, hepatic neoplasia in eight (40%). This means that neoplasia in extrahepatic sites was observed in 60% of the studies and there is insufficient evidence to reject all comparisons of neoplasia on the basis of dissimilarities in hepatocellular carcinogenesis alone.

There are no human trials showing an increased risk of cancer with any statin.

While this is strictly true, there is indirect evidence that should prompt a reassessment of cholesterol-lowering drugs, the statins included, under certain circumstances. The reason that studies of carcinogenicity are done in rodents is that it is not considered necessary to prove carcinogenicity in humans for such concerns to be raised. Evidence of carcinogenicity of hypolipidemics was mentioned for three classes of drugs -- in 1/2 studies of bile acid binders (cholestyramine resin and colestipol hydrochloride), 5/6 studies of fibric acid derivatives (clofibrate and gemfibrozil), and in 11/12 studies of HMG-CoA reductase inhibitors (lovastatin, pravastatin sodium, simvastatin, and fluvastatin sodium), but not for one study of niacin and one study of probucol. When relative exposures for single drugs in two classes were considered, the relative exposure in mg/kg was far lower for gemfibrozil than for lovastatin (10 mg/kg vs. 62.3-312 mg/kg, respectively), and was also lower, although the difference was not as great, for AUC measurements (0.7-1.3 vs. 1-4, respectively)[1]. Hence, evidence of carcinogenicity in rodents has been observed for these three classes of drugs, the relative exposures at which this occurred are considerably lower than those originally calculated, and for at least two specific drugs the carcinogenic dose in rodents is equal to the maximum recommended human dose. Weighing evidence for carcinogenicity requires consideration of the cumulative time of exposure in addition to actual doses employed. For asymptomatic persons with hypercholesterolemia, the cumulative exposure time to these drugs may be on the order of decades.

Neither article disputes that there is an association between very low cholesterol levels and increased risk of cancer. It has been established that persons with very low cholesterol levels have higher cancer death rates in cohort studies, but there is evidence that decreased cholesterol levels may precede a diagnosis of cancer by several years, and additional evidence that lowering cholesterol may promote rather than initiate carcinogenesis.[4,5,6] There is also evidence to indicate that the process of lowering blood cholesterol may itself be the culprit. Davey-Smith and Pekkanen performed meta-analyses using results of three clinical trials of dietary interventions and four clinical trials of drug interventions.[7] In both types of trials, the estimate of relative risk (RR) was suggestive of increased cancer mortality due to the intervention (RR=1.31, 95% confidence interval 0.92-1.86, and RR=1.33, 95% confidence interval 0.93-1.89, respectively), and there was no statistically significant difference between the two. Similar results have been reported elsewhere. This leaves open the question of whether carcinogenesis is related to effects of the drug or to the reduction of cholesterol.

According to the American Heart Association: "There is strong justification for prescribing these drugs for coronary heart disease patients and other individuals at high risk for developing heart disease... And patients should not discontinue the use of these drugs if their physician feels they can benefit from their use."

Neither Newman and Hulley nor Dalen and Dalton appear to disagree with this statement, because the benefits of cholesterol lowering appear to exceed the risks, at least among persons at high short-term risk of CHD. The controversy arises with respect to persons who do not meet this criteria, and for whom the benefits may not exceed the risks. If Newman and Hulley's findings are given little weight, the current benefit-risk equation for use of hypolipidemic drugs does not change, even when these drugs are used for asymptomatic persons with hypercholesterolemia. If their findings are given more weight, it would seem to give pause to the use of hypolipidemic drugs, particularly for asymptomatic persons with hypercholesterolemia when other treatment options, particularly diet and exercise, have not been exhausted. According to the U.S. Preventive Services Task Force, *Guide to Clinical Preventive Services*, "Decisions for high cholesterol should be based on at least two measures of cholesterol and assessment of the absolute risk of CHD in each individual...[including] the age of the patient, results of lipoprotein analysis, and the presence and severity of other risk factors for CHD. Initial therapy for patients with elevated cholesterol is counseling to reduce consumption of fat and promote weight loss in overweight persons. Benefits of drug therapy are likely to justify costs and potential risks only in persons at high risk of CHD."[8] We look forward to more debate on this issue.

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INFORMATION FOR CONTRIBUTORS

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A manuscript will be accepted for consideration with the understanding that is an original contribution, has never been published in its current form, and is submitted only to *Medicine and Health/Rhode Island*. An article should address a substantive issue of interest to the Rhode Island medical community, and be no more than 3,000 words in length and have no more than 20 references.

Submission Requirements

Manuscripts should be typewritten, double-spaced with liberal margins. Authors also are asked to provide the manuscript and computer-generated graphics on a floppy diskette, formatted in either Microsoft Word or Word Perfect. If possible, Macintosh disks should be saved in DOS format, using Apple File Exchange.

Illustrations and charts must be submitted in black ink on white paper. Laser-printed graphs are acceptable, provided they are printed at 300 DPI resolution.

Photographs must be in black and white, submitted on 5" x 7" glossy paper.

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Health by Numbers

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Jay S. Buechner, PhD and William J. Waters, Jr., PhD

Hospital Stays for Newborns in Rhode Island, 1993-1995

William H. Hollinshead, MD, MPH and Samara I. Viner-Brown, MS

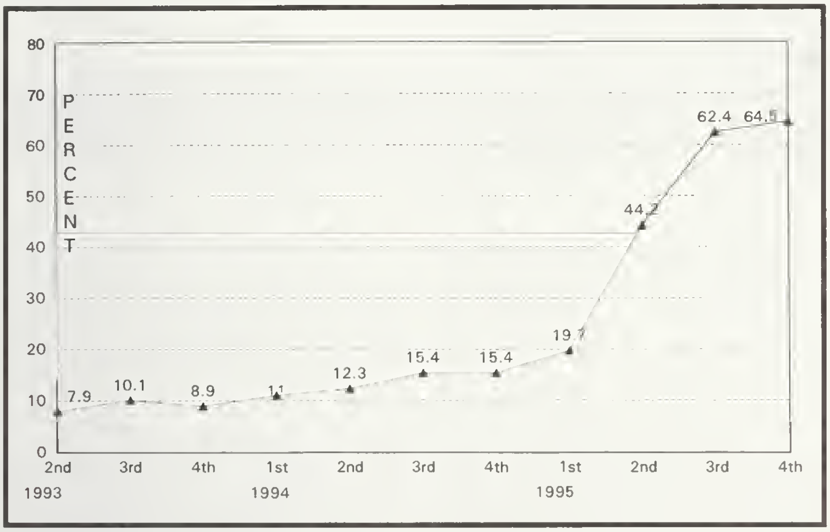


Figure 1. Short Newborn Stays by Quarter of Discharge, Rhode Island, 1993 - 1995

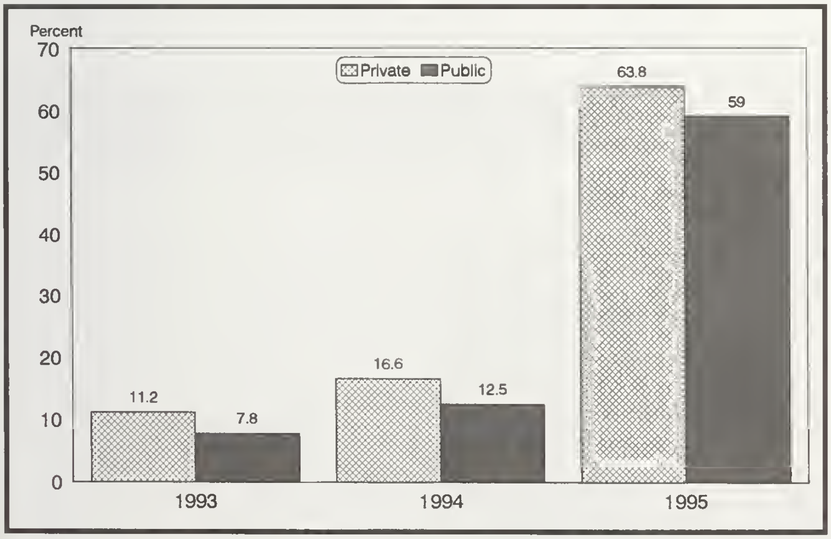


Figure 2. Short Newborn Stays by Insurance Status, Rhode Island, Third Quarter (July - September) 1993-1995

Dr. Hollinshead is Medical Director, Division of Family Health, and a clinical assistant professor, Department of Community Health, Brown University School of Medicine. Ms. Viner-Brown is Chief, Data and Evaluation, Division of Family Health.

Delivery of a newborn is the most common reason for hospitalization among persons under age 65. Only a few years ago, mothers and newborns remained in the hospital for several days, and observation, teaching, and recovery commonly occurred in the hospital. Recent data from Rhode Island's universal newborn screening system show a majority of infants now go home on the day of delivery or on the day after delivery — a dramatic change that has elicited wide public and professional interest.

METHODS

Data were obtained from the Universal Newborn Screening Program, which screens every baby born in Rhode Island for developmental risk factors. These data include date of birth and date of discharge from the hospital, as well as demographic items and source of health care coverage taken from the birth certificate worksheet. Since hour of discharge is not available, short newborn stays are defined as newborn discharges on the day of delivery or the day after delivery. Short stays defined in this way are all therefore less than 48 hours from delivery. (Note that this definition cannot be compared to the mother's length of stay in the hospital as measured traditionally, from day of mother's admission to day of her discharge.) The data described here are for vaginal deliveries and were analyzed on a quarterly basis. During the third

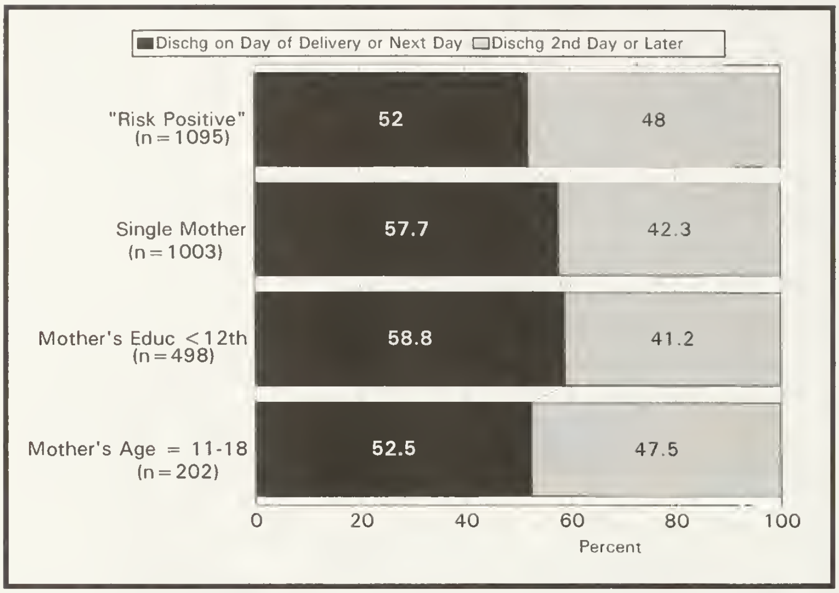


Figure 3. Selected Risk Factors of Newborns by Newborn Stay Group, Rhode Island, July - September, 1995

quarter (July - September) of 1995, there were 3,010 vaginal deliveries; the number of vaginal deliveries for the same months of 1993 and 1994 were 2,900 and 3,125, respectively.

RESULTS

Universal newborn screening data indicate that the prevalence of short newborn stays (discharged on the day of delivery or on the day after delivery) increased from 15 percent of vaginal deliveries during the period July through September 1994 to 62 percent in the same three months of 1995. (Figure 1). This change is seen among both privately insured patients (e.g., patients insured by Blue Cross, United Health Plans, etc.), and patients covered by public programs (primarily Medicaid, but also including CHAMPUS, unreimbursed care, etc.). (Figure 2).

These data also show that short stays are common among newborns whose parents are adolescents, or have limited education, resources, or family support. (Figure 3). Based on the Universal Newborn Screening Program's criteria, during the third quarter of 1995, 1,095 of these babies were identified as having two or more of thirteen developmental risk factors related to limited resources, nurturing challenges, and/or the infant's health, which makes them eligible for home visiting services from the Department of Health's Family Outreach Program. Of the 1,095 "risk positive" babies, 570 (52%) went home either on the day of delivery or on the day after delivery, including 558 with two or more factors related to poverty or nurturance challenges, 153 after limited prenatal care, and 20 with birth weights below 2500 grams (5 pounds, 8 ounces).

DISCUSSION

Hospitalization for delivery is unique, in that it involves two patients, and protects a critical normal event at the beginning of a lifelong relationship. With shrinking newborn stays, there is less time for observation, testing, education, and recuperation of mother and infant. Those concerns are heightened if the risks and needs of new parents have not been fully addressed in the prenatal period, or if problems arise at time of delivery, or if there is not strong ongoing support for the new mother and infant at home. On the other hand, a short newborn stay is safe and often appropriate if parents and professionals are involved in an effective system of comprehensive care that addresses these concerns before and after the hospitalization.

Rhode Island has a history of excellent maternity and infant care, and many resources to address the needs of parents and newborns. Health professionals, hospitals, health plans, community agencies, parents, and many others are working to adjust to short newborn stays in hospital. Together, we can build an even stronger system of care, which will recognize and address needs even before pregnancy begins, assure comprehensive risk-responsive prenatal and perinatal care, and support parent nurturance and the healthy development of all infants and children.

EDITOR'S NOTE:

The February Health By Numbers, "Oral Cancer in Rhode Island" was written by John P. Fulton, PhD, of the Rhode Island Department of Health, Division of Disease Control. We failed to attribute the article to Mr. Fulton and apologize for any confusion that may have resulted.

Vital Statistics

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Roberta A. Chevoya

Rhode Island Monthly Vital Statistics Report
Provisional Occurrence Data from the Division of Vital Records

Vital Events

	Reporting Period		
	Oct. 1995	12 months Ending with Oct. 1995	
	Number	Number	Rates
Live Births	1,277	13,915	14.0*
Deaths	807	9,709	9.7*
Infant	(10)	(101)	7.3#
Neonatal	(6)	(79)	5.7#
Marriages	882	7,289	7.3*
Divorces	265	3,637	3.7*
Induced Terminations	456	5,915	425.1#
Spontaneous Fetal Deaths	132	1,078	77.5#
Under 20 weeks gestation	(124)	(1,007)	72.4#
20 + weeks gestation	(8)	(71)	5.1#

* Rates per 1,000 estimated population
# Rates per 1,000 live births

Underlying Cause of Death

	Reporting Period			
	April 1995	12 Months Ending with April 1995		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	279	3,279	329.1	4,391.5
Malignant Neoplasms	210	2,431	244.0	6,869.0
Cerebrovascular Diseases	61	603	60.5	682.0
Injuries (Accident/Suicide/Homicide)	29	338	33.9	6,526.0
COPD	33	396	39.7	225.0

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.
(b) Rates per 100,000 current estimated population of 996,325.
(c) Years of Potential Life Lost (YPLL).

Note: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

Medicine & Philately

John T. Tierney

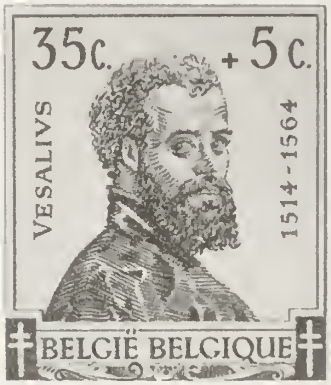


Figure 1.

Andreas Vesalius, Anatomist of Padua

Andreas Vesalius [Belgium, 1942, Scott B320][1],[2] was born in Brussels, Belgium in 1514 and died near the Mediterranean isle of Zante in 1564 (figure 1). As a young student he was said to be gifted in mathematics, language and vertebrate zoology. He enrolled in the University of Louvain [Belgium, 1975, Scott 939] from 1528 to 1533. The displayed stamp (figure 2) entitled, *Seat of Wisdom*, was issued on the 550th anniversary of the University.

In 1533 Vesalius transferred to the University of Paris to pursue his studies of medicine, remaining there until 1536 when he was forced to leave after the armies of Charles V invaded France. He then returned to Louvain to continue his studies of medicine.

Vesalius practiced medicine in Venice where he first met Johann Stephen von Calcar, a disciple of the great painter Tiziano Vercelli Titian. Calcar was to become Vesalius' collaborator and the artist responsible for drawing the superb woodcut illustrations of the immortal *De fabrica* as well as the drawings in other texts. At age 32 Vesalius was appointed professor of surgery and anatomy at Padua [Belgium, 1964, Scott 606], (figure 3). This appointment provided Vesalius with the necessary freedom to conduct autopsies and pursue his pioneering studies of anatomy and pathology. (Vesalius' courage in recording and reporting his anatomic observations would eventually lead to his dismissal.)

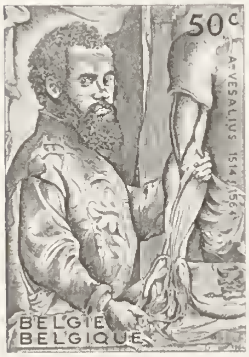


Figure 3.

In the 16th century Galen (130 - 201?) was the undisputed authority on anatomy and medicine [Yemen, 1966, Minkus 492[3]]. Galen had been born in Pergamon, Turkey and had studied medicine in Alexandria. After practicing in Pergamon for a few years, he then transferred to Rome, entering the inner circles as court physician. His extensive writings and physiologic experiments earned him the reputation as the successor to Hippocrates. But because autopsies were uniformly banned, many of his anatomic surmises were in error.

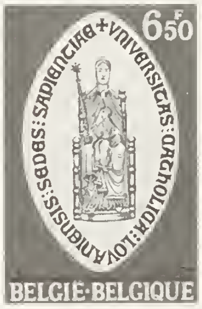
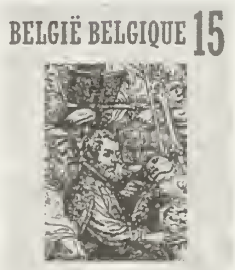


Figure 2.

Vesalius, through his University status, was provided with a measure of intellectual freedom. He continued his studies, based upon human autopsies that in 1543 culminated in the completion of his great text *De corporis humani fabrica libri septem*, popularly known as *Fabrica* [Belgium 1993, Scott 1507] (figure 4). The text consisted of 660 pages and over 300 magnificent illustrations produced by Calcar and others. In *Fabrica*, Vesalius identified over 200 errors in the writings of Galen. But since most of his contemporaries remained firm believers in the words of Galen, Vesalius was obliged to resign his academic post, becoming court physician to Charles V. The animosity directed at Vesalius by both the physicians and religious leaders was so intense, however, that he was forced to leave Venice.



De Humani Corporis fabrica

Figure 4.

In 1564 Vesalius undertook a pilgrimage to Jerusalem. On the return trip his ship encountered a major storm and sank, with all passengers and hands lost, near the coast of Zante (the island now known as Zakynthos.) On his tombstone in Zante is written the following: "Andreas Vesalius of Brussels; died on October 15, 1564 at the age of 50 during the trip from Jerusalem.

* * *

References:

1. A Scott number preceeded by a B indicates a semi-postal stamp which has two values on it; Scott B320 has both 35c and 5c. The higher value (35 centimes) represents the cost of the postage while the other (5 centimes) represents a mandated contribution to a selected charity. In this instance the surtax was used to help fight tuberculosis and the funds were forwarded by the national postal service to appropriate tuberculosis control agencies. The United States does not use semi-postal stamps although many European countries do.
2. Scott's is an internationally recognized stamp catalog with a numbering system permitting easy identification. The numbers in brackets are those assigned to the cited philatelic issues.
3. The Minkus Catalog, also published in the U.S., is similar to the Scott Catalog with a different numbering system.

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POINT OF VIEW

Informed Consent: A Primer for Health Care Practitioners

David A. Wollin, Esq., and Joseph Avanzato, Esq.

David A. Wollin, Esq., and Joseph Avanzato, Esq., are principals of Adler Pollock & Sheehan Incorporated in Providence, Rhode Island, and are members of the firm's health care practice group.

The doctrine of informed consent, which has guided medical decision-making for decades, guarantees that a patient has a right to make an informed decision about his or her medical treatment. As Justice Benjamin Cardozo observed long ago, the doctrine is based on the notion that "[e]very human being of adult years and sound mind has a right to determine what shall be done with his own body."

Primarily, the informed consent doctrine in Rhode Island has evolved in the courts. In recent years, however, federal and state governments have augmented the common law by enacting specific consent requirements in certain situations, such as in the case of advance directives, patient transfers, human experimentation, and conflicts of interest.

THE COMMON LAW DOCTRINE OF INFORMED CONSENT

RHODE ISLAND

The Rhode Island Supreme Court in *Wilkinson v. Vesey*, the seminal case on the informed consent doctrine, observed that the "keystone" of the doctrine is "every competent adult's right to forego treatment, or even cure, if it entails what for him are intolerable consequences or risks however unwise his sense of values may be in the eyes of the medical profession, or even the community."

ABBREVIATIONS USED

AIDS	Acquired immune deficiency syndrome
COBRA	Consolidated Omnibus Budget Reconciliation Act
HIV	Human immunodeficiency virus
IRB	Institutional Review Board

The informed consent doctrine imposes upon a physician the duty to inform his or her patients about the risks involved in a proposed course of treatment and the alternatives to the treatment. The duty is separate and distinct from a physician's responsibility to diagnosis and treat a patient's illness properly.

In *Wilkinson*, the Rhode Island Supreme Court ruled that the patient has a right to full disclosure of all "material" facts. Materiality is defined by an "objective" standard: "Materiality may be said to be the significance a reasonable person, in what the physician knows or should know is his patient's position, would attach to the disclosed risk or risks in deciding whether to submit or not to submit to surgery or treatment." However, a physician need not disclose risks that are likely to be known by the average patient or that are in fact known to the patient because of a past experience with the treatment in question.

A physician may be held liable for negligence if a jury finds that the communication to the patient was unreasonable or inadequate. To prove negligence, a patient need not present expert testimony reflecting a community standard of disclosure. The Rhode Island Supreme Court held in *Wilkinson* that a patient's right to make up his mind "should not be delegated to a local medical group — many of whom have no idea as to his informational needs."

Nonetheless, the community standard is relevant in negligence cases. A physician may introduce evidence of conformity with the community standard as evidence of a lack of negligence. On the other hand, a patient may produce expert testimony on the community standard of disclosure to show that a physician failed to inform properly about the risks of a particular procedure.

DISCLOSURE OF RELEVANT INFORMATION

The doctrine of informed consent requires a physician to disclose a variety of information to a patient. Although it is difficult to generalize about the appropriate information that needs to be disclosed in every case, the following information normally will be necessary:

First, a physician must adequately describe the patient's diagnosis, including the medical steps that were taken to arrive at the diagnosis.

Second, a physician must inform the patient of the nature and purpose of the proposed treatment to address the medical problem, including the benefits to be reasonably expected.

Third, and most importantly, a physician must discuss the risks of the proposed treatment. Specifically, a physician should discuss the severity of the risk, the likelihood of its occurrence and the patient's susceptibility to an adverse outcome. Thus, courts have held that physicians have an obligation to disclose the risk of death or serious disablement, even if very small. Similarly, a potential disability that dramatically outweighs the potential benefits of treatment may require appropriate discussions with the patient.

Fourth, a physician should disclose alternative treatments that are generally available and recognized within the medical community, the risks and consequences of such alternatives and the probability of success. Indeed, a few courts outside of Rhode Island have held that alternatives should be dis closed even if they would be more hazardous.

Fifth, a physician has an obligation to disclose to the patient both the prognosis with treatment and, in certain cases, the prognosis if treatment is rejected. A California court has gone so far as to rule that a physician has a duty to disclose the consequences of the patient's decision to decline a procedure or test that the doctor views as valuable.

EMERGING ISSUES ON INFORMED CONSENT

Physicians should expect to see future cases raising the issue whether they should inform a patient about the success and failure rates of performance of particular procedures. One court has suggested that a physician should disclose both the general statistical success rate for a given procedure, as well as his or her particular experience with the procedure.

Moreover, courts will likely address whether physicians have an obligation to inform his or her patients about a particular impairment (such as HIV infection) that might affect performance and success rate. A New Jersey court has ruled that a hospital had an obligation to disclose to a patient that a staff surgeon who performed an invasive procedure was suffering from AIDS.

Finally, courts are also beginning to address whether physicians have an obligation to disclose their research and economic interests in treating a particular patient. A California court has ruled that a physician must disclose his research or economic interests unrelated to patient health in obtaining consent to medical treatment.

STATUTORY DUTY OF INFORMED CONSENT

In addition to the common law doctrine of informed consent developed in the courts, federal and state governments have enacted specific statutory and regulatory consent requirements in four principal areas — advance directives; patient transfers; human research; and conflicts of interest.

ADVANCE DIRECTIVES

The Patient Self-Determination Act requires hospitals, skilled nursing facilities, home health agencies, hospice programs, and health maintenance organizations that receive Medicare or Medicaid funding to provide each patient with written information about his or her right under state law to make decisions concerning medical care, including the right to accept or refuse medical treatment, to execute advance directives, and to have access to the written policies of the health care facility respecting the implementation of such rights. Under the Act, health care facilities must document in each patient's record whether he or she has signed an advance directive, educate their staff concerning its policies and procedures on advance directives, and provide for community education regarding advanced directives.

> *Every human being of adult years and sound mind has a right to determine what shall be done with his own body.*

PATIENT TRANSFERS

The Consolidated Omnibus Budget Reconciliation Act or "COBRA" requires that health care facilities that seek to transfer patients from one hospital to another discuss the transfer with the patient and receive his or her authorization prior to any transfer. The hospital may not transfer unless the patient, after being informed of the hospital's obligation under the law and the risk of transfer, requests in writing transfer to another medical facility.

HUMAN EXPERIMENTATION

The United States Department of Health and Human Services has promulgated federal regulations governing research involving human subjects entitled "Basic HHS Policy for Protection of Human Research Subjects." Subject to certain exceptions, the policy applies to all research involving human subjects conducted, supported or otherwise subject to regulation by any federal department or agency. The Food and Drug Administration's regulations parallel the Department's regulations.

At the heart of the federal regulations is the Institutional Review Board or "IRB," which must be established at every institution to review research conducted at that institution. No federally-funded research may be conducted at an institution without the IRB's approval. The IRB is also empowered to conduct continuing review of the research it has approved, and must review each continuing research protocol once each year. An IRB is authorized to suspend or terminate approval of research that has been associated with unexpectedly serious harm to subjects. In order to approve research, the IRB must determine that the risks to subjects are minimized and reasonable in relation to anticipated benefits and the importance of the knowledge that may reasonably be expected to result; the selection of subjects is equitable; informed consent will be sought and documented from each prospective subject or his or her legally authorized representative; the research plan makes adequate provision, when appropriate, for monitoring the data collected to ensure the safety of subjects; and there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

No investigator may involve a human being as a subject in research covered by this policy unless he or she has obtained the legally effective informed consent. An investigator must seek such consent only under circumstances that provide the prospective subject sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject must be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or to release or appear to release the investigator, the sponsor, the institution or its agents from liability for negligence.

In seeking informed consent, the following information must be provided to each subject: (1) a statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental; (2) a description of any reasonably foreseeable risks or discomforts to the subject; (3) a description of any benefits to the subject or to others which may reasonably be expected from the research; (4) a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject; (5) a statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained; (6) for research involving more than minimal risk, an explanation as to whether any compensation will be provided and as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained; (7) an explanation of whom to contact for answers to pertinent questions about the research and research subject's rights, and whom to contact in the event of a research-related injury to the subject; and (8) a statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waives the requirements to obtain informed consent, provided the IRB finds and documents that the research involves no more than minimal risk to the subjects; the waiver or alteration will not adversely affect the rights and welfare of the subjects; and the research could not practicably be carried out without the waiver or alteration.

Conflicts of Interest

Under Rhode Island law, a physician who has an ownership interest in any health facility, laboratory or equipment not on the premises must, in writing, make full disclosure to his or her patients of the ownership interest in the facility or therapy prior to utilization. The written notice must state that the patient has free choice either to use the physician's proprietary facility or therapy or to seek needed medical services elsewhere.

Exceptions to the Doctrine of Informed Consent

Courts have recognized several exceptions to a physician's duty to obtain informed consent before performing medical treatment.

Emergencies

The Rhode Island Supreme Court in *Miller v. Rhode Island Hospital* ruled that the doctrine of informed consent does not apply in cases of emergency. The exception comes into play when the patient is unconscious or otherwise incapable of consenting, and the harm from a failure to treat is imminent and outweighs any harm threatened by the proposed treatment. As the court observed, "When a genuine emergency of that sort arises, it is settled that the impracticality of conferring with the patient dispenses with need for it."

Even in emergency situations, however, the physician should, if practical, attempt to secure a relative's consent. If time is too short to accommodate such consultation, the physician may proceed with the treatment without obtaining the appropriate consent.

Therapeutic Privilege

Rhode Island courts have also recognized that a physician does not have to provide information to a patient when he feels such information would complicate the patient's medical condition or render him unfit for treatment. As one federal court has noted, "It is recognized that patients occasionally become so ill or emotionally distraught on disclosure as to foreclose a rational decision, or complicate or hinder that treatment, or perhaps even pose psychological damage to the patient. Where that is so, the cases have generally held that the physician is armed with a privilege to keep the information from the patient." However, the privilege does not accept "the paternalistic notion" that the physician may remain silent simply because "divulgence might prompt the patient to forego therapy the physician feels the patient really needs."

Waiver of Consent

Some courts have indicated that patients may waive their right to give an informed consent. Such a waiver, which should be in writing, must be made freely and with full knowledge of what is being waived.

Ensuring Compliance with the Informed Consent Doctrine

To ensure compliance with the informed consent doctrine, a physician should set forth in detail the discussions he or she had with a patient about each of the factors discussed above. It is normally not sufficient for a physician to state simply that the risks were explained to the patient.

Although there is no general requirement, a consent to medical treatment should be obtained in writing as well. Hospitals use consent forms at several points throughout the patient's care. A written consent that specifically memorializes the discussions a physician had with a patient will have significant probative weight in the event legal action is brought. Further, the patient's signature reinforces the patient's understanding of the discussions that occurred.

Normally, a consent form will be treated as presumptively valid consent to the treatment, with the burden on the patient to rebut the presumption. However, courts have shown a reluctance to enforce overly broad, "boilerplate" consent forms, which fail to provide specific information to patients about the risk of particular procedures.

Correspondence:

Readers who wish to obtain a list of references relied upon for this paper may contact:

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THE RHODE ISLAND MEDICAL JOURNAL

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PROVIDENCE, R.I., JANUARY, 1917

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NINETY YEARS AGO

APRIL, 1906

The lead article, by George S. Matthews, MD, describes his four-month experience in the diagnosis and treatment of 22 consecutive cases of typhoid fever, 19 of whom were male. The author first describes the prodromata, consisting mainly of headache, anorexia and nausea. Rose spots were found in 21 of the 22 cases. The spleen was palpable in 15 and the white blood cell count tended to be low except when intestinal perforation occurred or when abscesses developed elsewhere in the body. Diarrhea was prominent in 12 cases. Urine analysis revealed some albumin in 19 cases. Four cases exhibited relapse. Nearly all were toxemic; and one definite and one possible perforation were recorded. Treatment was limited to sedation, cardiac tonics and tubbing when temperatures rose excessively. A milk diet was generally employed.

George D. Hersey, MD describes a 24 year old male Canadian inpatient with typhoid fever who suddenly developed abdominal pain and rigidity. The patient was operated upon using ether anesthesia. About 12 inches from the cecum an ileal perforation was found and repaired. Four drains were inserted and the patient was returned to the ward. Four weeks later the wound healed and the patient was discharged 45 days after surgery.

The minutes of the December, 1905, meeting of the Providence Medical Association are summarized. Most of the meeting was devoted to an extended discussion moderated by Dr. Charles V. Chapin on the etiology and prevention of tuberculosis. Chapin emphasized the importance of early recognition, the use of stringent hygienic measures with each patient and the reporting of such cases to central authorities. He pointed to the world-wide reduction in tuberculosis morbidity and mortality, saying that medicine cannot claim a major role in this. The ensuing discussions were candid and earnest, touching upon such related issues as the need for further sanitorium beds, a better reporting system and the dubious role of the insurance companies in influencing diagnostic decisions reached by physicians. During the January, 1906, meeting, various papers relating to adenoid/tonsillar surgery were presented and discussed.

A separate report on the means by which cases of tuberculosis should be reported to the Health Department of Providence is provided.

Dr. Chapin's summary health report is published. He notes that the death rate for the preceding year (1905) is the lowest in his experience. The most notable reductions occurred with infectious diseases. Deaths from tuberculosis dropped to 318 and deaths from pneumonia, 410. Diarrheal disease caused 244 deaths (58 less than the preceding year) and there were 61 deaths from diphtheria. Scarlet fever deaths were reduced from 43 in 1904 to 18 in 1905.

FIFTY YEARS AGO

APRIL 1946

Edward Damarjian, MD presents a series of 100 consecutive brachial blocks performed by the anesthesiology service of a military hospital. All of the patients in this series were on the orthopedic surgery service. The author concludes: "For repeated successful blocks, it is necessary that an operator have a good knowledge of the anatomy of the brachial plexus and its exact peripheral distribution. Furthermore, paraesthesias must be elicited to insure proper block anesthesia in every case. We feel that this type of anesthesia eliminates many of the hazards that would be encountered in inhalation or intravenous anesthesia. Brachial blocks have been popular among the patients of this hopsital and many requests are made for this type of anesthesia in preference to the popular Pentothal." No significant complications were encountered.

Out-patient electric convulsive therapy for psychiatric conditions is described by Laurence A. Senseman, MD. He first details the history leading up to this form of therapy. The first observations were made by Sakel who noted, in 1928, that insulin shock alleviated some of the more distressing features of psychoses particularly severe depression. In 1934 Meduna introduced metrazol convulsive therapy and in 1938, Cerletti and Bini achieved similar results by passing an electric current through the brain. The author then describes, in detail, the patient-preparation and electro-convulsive technics that he employs, giving details and outcomes on 30 recent cases. About one-third showed substantial improvement and most were somewhat improved. He concludes: "Electric shock therapy can safely be given on an out-patient basis. Depressed patients show the most favorable response in this series of cases."

Following the release of substantial amounts of dried blood plasma by the armed services, a program of free distribution has been undertaken in Rhode Island. An article describes the details of this program and outlines the indications for the transfusion of whole blood, plasma or serum.

Rhode Island Hospital refresher courses for veteran-physicians (first in pediatrics) are described by Stanley S. Freedman, MD.

Ringworm of the scalp is discussed by William Cohen, MD and Carl Sawyer, MD.

The 135th Annual Meeting of the Rhode Island Medical Society is described. Of significance was a panel discussion on the activities of Rhode Island physicians in the military serving in the China-Burma-India Theater of war. Papers by Frank B. Cutts, MD, J. Murray Beardsley, MD and Irving A. Beck, MD were presented.

TWENTY FIVE YEARS AGO

APRIL, 1971

Max H. Parrott, MD of the American Medical Association discusses current health care problems, ranging from quality of care to physician competence, and offers certain possible approaches.

Russell Roth, MD, also from the American Medical Association, highlights the concerns of the AMA with regard to currently considered legislative proposals for a national health insurance.

Mark Hochberg, MD and Henry T. Randall, MD present their findings regarding cholesterol absorption following extensive experimental small bowel resection in dogs. The drastic reduction in circulating cholesterol, following this procedure, prompts them to consider such an intervention in humans with intractably high cholesterol levels.

John R. Stuart, MD and William S. Klutz, MD describe three cases of rectal obstruction cause by silent carcinoma of the prostate. Prompt recognition and treatment is advised.

Marcus McCorison describes medical collections at the American Antiquarian Society.

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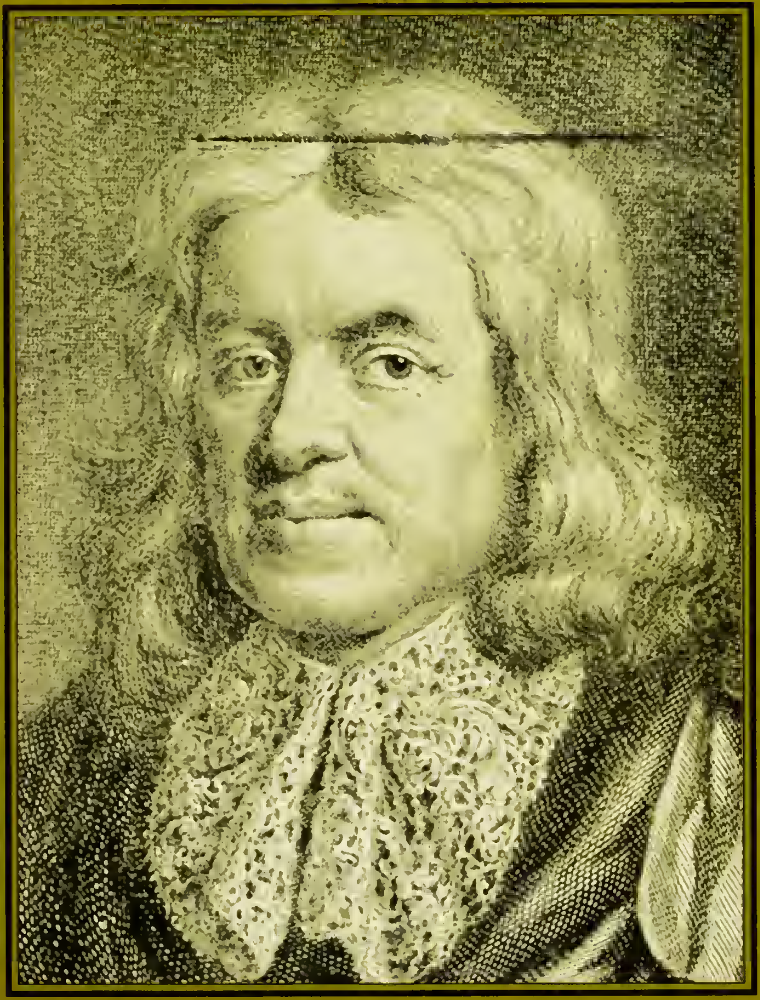

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Cover: Etching of Dr. Thomas Sydenham.

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COMMENTARIES

Advances: Part II

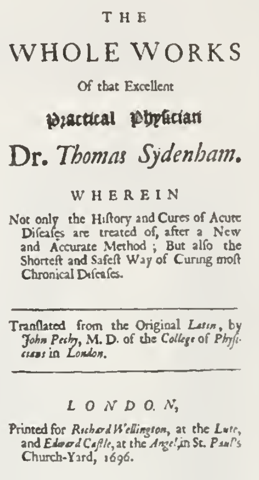
Over the last decade, medical advances seem to have come fast and furiously. We particularly recognized this when we began to compile our annual review of "recent medical advances." To accommodate the many important recent advances and to provide our readers with a thorough review of new treatment possibilities and those showing promise for the future, we have dedicated this issue to the continuation of our March edition.

The articles featured in this issue clearly demonstrate the positive effects of molecular biology and molecular genetics on the practice of medicine. As our knowledge has grown in these fields, so too have we been able to apply what we have learned and put it into practical application as diagnostic and therapeutic tools.

This issue contains a discussion of the importance of molecular and immunologic events in the pathogenesis, diagnosis, and treatment of HIV disease. The importance of the Diabetes Control and Complications Trial, adrenal cortical disease, pheochromocytoma, reproductive endocrinology, and neuroendocrinology are some of the topics covered by the authors of the comprehensive endocrinology article.

In the cardiology update, an extensive review is provided which includes atrial fibrillation and its therapy, interventional coronary revascularization, especially as it has been examined by many cooperative trials (with somewhat helpful acronyms), the importance of primary angioplasty in myocardial infarction and new treatments for obstructive hypertrophic cardiomyopathy.

The first page of Dr. Thomas Sydenham's collected works, the English translation of which was published in 1696.



THE
WHOLE WORKS
Of that Excellent
Practical Phyſician
Dr. *Thomas Sydenham.*
WHEREIN
Not only the Hiſtory and Cures of Acute Diſeaſes are treated of, after a New and Accurate Method; But alſo the Shorteſt and Safeſt Way of Curing moſt Chronical Diſeaſes.

Tranſlated from the Original *Latin*, by *John Pechy*, M. D. of the *College* of *Phyſicians* in *London.*

LONDON,
Printed for *Richard Wellington*, at the *Lute*, and *Edward Caſtle*, at the *Angel*, in St. *Paul's* Church-Yard, 1696.

The issue is rounded out with a thorough discussion of fibromyalgia, including recent advances in its diagnosis, treatment, and patient education.

We are grateful to the authors of these articles and those that appeared in the March edition. Through their efforts, many of us will be able to exploit the information gleaned through these articles for the benefit of our patients.

Fred J. Schiffman, MD

Joining the Internet Revolution

The internet is a connection of computers across the world, creating a huge network. People with personal computers can access this network to send e-mail (electronic mail), participate in discussion on newsgroups, and view documents on the world wide web.

E-mail is a cross between regular mail and answering machines. Like regular mail, it can be written at one's leisure and read quickly. Like an answering machine, the transmission is almost instantaneous. There are other benefits of e-mail, which include the ability to do multiple mailings and to attach binary files to a message. E-mail has become my personal message secretary. I currently use e-mail to keep in touch with several of my clinical and basic science teachers. I've asked them questions and set up appointments through this medium.

Newsgroups are another phenomena of the internet. They can be thought of as a form of public e-mail. For example, I can send a message publicly announcing that I am selling my stethoscope because I don't know how to use it. Many people can access this message and a potential buyer might write back inquiring about the type of stethoscope. I would answer that it is a Littman Cardiology II, black colored, and hardly used. Other people can read these messages and participate in the discussion. Perhaps a Littman salesman may read the message and offer a refund. An astute medical student might offer advice on how to use the stethoscope (i.e., it has two sides, you need to turn it to the right side to use it). On a more serious note, I've participated in a newsgroup run by a pharmacology professor at Brown. He posts clinical cases and has us post solutions, and then he offers his comments on-line.

The world wide web (WWW) is one of the newest additions to the internet. It began with hypertext, which has been around since I was in middle school (early 1980's). Hypertext is similar to reading a word-processing file with some of the words highlighted. When one clicks on a highlighted word, the computer jumps to another screen displaying the highlighted topic in greater detail. Next it became possible to jump to information on someone else's computer when the highlighted text was clicked. Voila! The world wide web was born.

The hypertext language evolved to link highlighted text with other text, pictures, and sounds on the same computer or on another computer linked by the internet. One can now navigate from one computer to another by "mouse clicks" through these modern hypertext documents, weaving a pathway that appears like a web. Even newer additions to the world wide web include links to e-mail addresses, newsgroups, and videos. For many people, the world wide web is the most exciting – and the most addicting – part of the internet.

The list of available topics is tremendous. Some popular uses of the net include previewing movies and songs, reading or hearing the news and weather, using the TV guide, playing the stock market , using Medline, and, of late, buying merchandise from toothbrushes to houses. Some magazines and journal also have a world wide web format, including *Medicine and Health/ Rhode Island.*

If you'd like to see it in a different format on the world wide web, our address is:

http://biomedcs.biomed.brown.edu/
RIMedicine/RIMedicine.html

When accessing it, please be sure to pay attention to the capital letters indicated above. They're important!

Several of Brown's Medical School functions also have web pages, including the Emergency Department, Plastic Surgery, Psychiatry, Obstetrics/ Gynecology, and Affinity groups. These can be found via the main Brown web pages (http://www.brown.edu) or through the various search engines accessible through the internet. It is possible to write a world wide web document using software that has recently become available or by reading one of the many books on web publishing. These documents could then be stored on the internet server.

How can you access the internet? If you have a Brown affiliation, Brown provides access without any access fees that are applied by services such as America On-Line, CompuServe, and Prodigy. You will need a computer, a fast modem (9600 bauds or better), a telephone line, a good chunk of time, and friends who can help set up the software and connection. Brown has a crew of knowledgeable consultants and printed material to help its members get started.

A decade ago, I used to claim that the world belongs to those who can type – anticipating the computer revolution. Now I believe that the world will belong to those who can type e-mail and navigate through the world wide web.

GLOSSARY

click – a method of activating a function on the computer by means of a keyboard, mouse, or other pointer device.

e-mail – electronic mail. Mail is typed into one computer and then sent to another computer via the internet.

hypertext – a type of document that provides access to other documents by clicking on highlighted text or pictures.

server – a computer provides access to the internet and stores e-mail, newsgroups and web pages.

network – a group of computers hooked up together with the capacity of sharing files and peripherals.

newsgroups – a public posting of messages that can include announcements, advertisements, and arguments. People can reply to these postings and some newsgroups are moderated and distributed by e-mail.

on-line – connected to the internet.

search engine – a web site that contains a database of other web pages, and one can search the database by keyword or topic.

web page – world wide web document.

web site – loosely defined, as a collection of web documents with a single theme.

world wide web (WWW or web) – a collection of multimedia documents on the internet which can be accessed in a point or click fashion. These documents are read by web browsers such as Netscape.

Calvin Lee

Calvin Lee is a third year medical student at Brown. He maintains the Medicine and Health/Rhode Island web pages. Comments about this essay and the electronic version of the journal can be sent to Calvin _Lee@Brown.edu. He transmitted this commentary via e-mail.

ON-LINE

Thanks to the tremendous effort of Calvin Lee, a third year medical student at Brown and a member of our editorial advisory board, *Medicine and Health/Rhode Island* is now available on the internet. We would like to publicly acknowledge the time and attention given to this task by Calvin, who already has a full and busy schedule. We also would like to express our appreciation to Susan Luckel of Brown's computer department, who helped Calvin over some of the rough spots in getting us up and running "on the net," and who maintained the journal by herself on the net for the past few years.

Through the efforts of these individuals, you may now find Medicine and Health/Rhode Island at:

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Darlene Trew Crist

The Puritan Physician from Dorset

In the decades succeeding the devastating bubonic plague of the mid-14th century, historians had recorded episodes of a curious dancing mania in many west European communities. At odd times, seemingly healthy people joined hands to enter into an arrhythmic cavorting which lasted for hours until - incoherent, incontinent and indecorous - they fell senseless to the ground. Their uncoordinated, paroxysmal movements were less a dance and more a series of graceless, jerking motions as though they were marionettes manipulated by invisible strings. Observers affirmed that the gamboling participants were governed by satanic spirits.

These bizarre episodes first centered in western Germany and then seemed to spread in epidemic fashion. They had first been called St. Johannes' Dance since John the Baptist was the protector of those afflicted with epilepsy and related movement disorders. Others called it St. John's chorea [from the Greek, *choros*, meaning a dance, as in the word choreography.] The choreic disorder spread to Saxony and northern France by the early 15th century and its victims frequently sought relief at the local shrine of St. Vitus, in Zabern. [Vitus was believed to be a fourth century Sicilian youth mentioned briefly - and without detail - in the writings of St. Jerome. Oral tradition, however, asserts that he was the son of a heathen Roman senator and that he was secretly converted to Christianity at age seven by his nurse. This outraged Valerian, then governor of Sicily, who used torture to force Vitus to relinquish his beliefs. An angel finally liberated both Vitus and his nurse, bringing them to the Italian mainland where Vitus preached to the multitudes and performed miracles including the healing of Emperor Diocletian's mortally ill son. Vitus was nonetheless proclaimed a sorcerer and was then cast into a cauldron of molten lead. He is said to have survived this event, but the circumstances surrounding his ultimate death remain obscure. His remains were eventually conveyed to Paris in the year 775; and thence to Saxony in 836. St. Vitus was then named the patron saint of Saxony [where his relics are situated], Bohemia [where the great cathedral of St. Vitus, in Prague, may be seen], as well as Sicily [his presumed place of birth.] Before his encounter with boiling lead, he is said to have prayed that the Lord spare those with nervous ailments. Thus Vitus eventually supplanted John the Baptist as the patron saint of those burdened with uncontrolled movements known by the 15th century as *morbus Sancti Viti*, and known today as St. Vitus' Dance.

In 1685, four years before his death, Thomas Sydenham described a malady of childhood in these words:

> "Chorea Sancti Viti is a sort of convulsion, which chiefly invades boys and girls from 10 years of age to puberty; first it shews itself by a certain lameness or rather instability of one of the legs which the patient drags after him like a fool; afterward it appears in the hand of the same side . . . which he can by no means keep the same posture for one moment. If a cup of water be put into his hand he represents a thousand gestures, like jugglers, before he brings it to his mouth; for whereas he cannot carry it to his mouth in a straight line, his hand being drawn hither and thither by the convulsion, he turns it often about some time, till at length happily reaching his lips, he flings it suddenly into his mouth and drinks it greedily as if the poor wretch were designed only to make sport."

The disorder is now called Sydenham's Chorea or chorea minor [thus distinguishing it from chorea major or Huntington's disease.] Both the dancing mania and Sydenham's chorea share the name of St.Vitus' dance but it is most doubtful that they are related by any common pathophysiologic feature. The dancing mania, more likely, was a manifestation of some shared hysteria and is probably akin to such bizarre, inexplicable phenomena as tarantulism in southern Italy, the "leaping ague" in 19th century Scotland or some acts of religious exaltation seen with the early Shakers or the French *convulsionaires*. Haggard [1] believed that the dancing mania represented a response to social despair and that ". . . their dance was as the scream, the sudden movement that gives relief from long pent-up emotion." Sydenham's chorea, on the other hand, has been firmly recognized as a transitory affliction of childhood closely associated with rheumatic fever and considered by neuropathologists as the clinical face of rheumatic encephalopathy. And as the incidence rate of rheumatic fever has fallen dramatically in the last half century, so too has the frequency of Sydenham's chorea. Today's pediatrician only rarely encounters the involuntary facial grimaces, or the aimless, uncoordinated, abrupt [and sometimes violent] limb and trunk movements characteristic of the disease. Wilson [2] once observed that ". . . the choreic child is punished thrice ere his condition is recognized – once for general fidgetiness, once for breaking crockery, and once for making faces at his grandmother."

Thomas Sydenham, who defined this pathologic fidgetiness, was born in 1624 to a prosperous Puritan family in Wynford, England. He attended Oxford University for less than a year before volunteering for duty in Cromwell's cavalry to fight the Royalists. He bore arms for four strife-filled years before returning to his university studies which culminated in a bachelor's degree in medicine in 1646. London then beckoned him; and for four busy decades – which witnessed the Restoration, the Great Fire of London and the Great Bubonic Plague – Sydenham conducted a flourishing practice based upon the novel thought that "the art of medicine was to be properly learned only from its practice." In the course of these years his prolific writings included the first clinical descriptions of scarlet fever, pleurisy, chorea minor, hysteria and particularly the disease with which he was personally afflicted: gout. His writings established him eventually as the greatest student of the natural evolution of illnesses and his meticulous descriptions were models of expository clarity for future generations of clinicians. He was an early advocate of Peruvian Bark [quinine] and laudanum. And despite his reputation as the father of bedside clinical medicine, Sydenham was neither a scholar nor an experimentalist. He deplored any references to the medical classics, regarding them as withered remnants of fanciful dogma. All of his writings were initially in English and only then translated to Latin. Nor did he have much respect for basic sciences, regarding them as irrelevancies. He was, for example, a contemporary of William Harvey, but never saw fit to meet with the great physiologist.

During his lifetime, the man who is now called the English Hippocrates, had not been accorded a single hospital staff appointment, was never chosen to grace any medical school faculty, and was not accorded fellowships either to the Royal College of Physicians or the Royal Society. Such was the blindness of seventeenth century English medicine. In possible expiation, there is now a grand marble bust of Thomas Sydenham enhancing the front lobby of the Royal College of Physicians. It faces the side windows, however, so that his unblinking gaze neither embarrasses nor causes the current Fellows to fidget as they enter.

Stanley M. Aronson, MD

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A Rose By Any Other Name . . .

In 1676 Thomas Sydenham published a brief description of a febrile exanthem, distinguishable from measles, which he called Scarlet Fever. It was an acute, communicable disorder, occuring mainly in children, " . . . with rigors and shiverings. Afterwards, however, the whole skin becomes covered with small red maculae, thicker than those of measles, as well as broader, redder and less uniform. They last for two or three days and then disappear." His bedside experience led him to conclude that the disease presented in three forms: *Scarlatina simplex*, the commonest and most benign form; *Scarlatina anginosa*, associated with intense pharyngitis, sepsis, delerium and exhaustion; and *Scarlatina maligna*, the rapidly fatal form.

For some 140 years following Sydenham's inaugural description scarlet fever remained a major source of morbidity and mortality in children and young adults, accounting for 5 to 7% of all deaths. In Providence, for example, Chapin collected epidemiologic data on 17,625 cases over a 40 year interval, with 1,039 deaths, a case fatality rate of 5.9%. He noted, however, that this rate was not constantly maintained. At the beginning of his observations, in 1880, the rate was 11% and by the 1920's it had dropped to 1.8%. The incidence rate of the disease had also fallen, but not as dramatically. The character of this disease, caused by a strain of hemolytic streptococcus, has indeed changed, not only in Providence but in urban centers throughout the world. By 1970 physicians were no longer required to report the disease and by the 1980's fewer than 10 deaths per year were recorded in the United States. There have been no scarlet fever deaths in Rhode Island for many decades.

There are many puzzles which surround the disease, one small one being: Why scarlet? Why not crimson, carmine, rose or just plain red ? Rarely, indeed, are illnesses formally defined in terms of color. Yellow jaundice, rubella and black plague, perhaps, but few others. Priority in the use of this color is found in Lancelotti's 1575 paper wherein he calls the disease *scarlatina* from the Italian *scarlatto* which is borrowed from the Arabic *siqillat* [meaning a seal] which, in turn, is borrowed from the Latin *sigillum*, diminutive of *signum* meaning a sign. In antiquity, scarlet was a highly prized dye used in the production of expensive fabrics as well as the coloring agent in seals placed upon important documents. The pigment was extracted from the body of a Near East insect, *Coccus ilicis* which is similar to the western hemisphere cochineal bug, *Coccus cacti*, the source of the dye, carmine.

The name, scarlet, appears in various Scriptural contexts. Most frequently, it describes cloth of great splendor and cost [Gen 38:28, Joshua 2:18] often used in priestly vestments and tabernacle furnishings [Exod 25:4, 28:5-6]. In Proverbs [31:21] the household of "the good wife" is "clothed in scarlet." The atmosphere around the word chills somewhat in Isaiah [1:18], where the color becomes metaphoric for wickedness: " . . . though your sins are like scarlet, " And in Revelation [17:1] we read of a woman, upon a scarlet beast, arrayed in purple and scarlet, "and in her hand a golden cup of abominations and the impurities of her fornication."

By the middle ages, the dual meanings of scarlet are well-established: as the color of grandeur and royalty ["the king's scarlet"] and as the defining color of venery and harlotry. Shakespeare talks of "scarlet indignation" but also of "a scarlet sin" and "foul sins, scarlet iniquities."

To Hawthorne's 19th century New England, a green letter or a lavender letter would have meant nothing to a Bible-literate readership; a scarlet letter, however, brought forth images of adultery and sin; and Hester Pryne was then obliged to wear a Scarlet Letter, through numberless editions, identifying her shameless adultery. And a century later when Hilaire Belloc wrote his own epitaph, he stated: "When I am dead, I hope it may be said: His sins were scarlet but his books were read."

Scarlet continues to waver in meaning between the fallen harlot [eg, the woman in red] and the less pejorative sense of excessive floral display and luxury [eg, the Scarlet Pimpernel.] In general, though, reds and shades of red tend to lean more closely to the realm of the outcast, the disenfranchised and the wicked [eg, a crimson reputation, the scarlet whore, the red light district.] Carmine, another shade of red, becomes a woman's name [eg, Carmen, the capricious temptress in Bizet's opera. Women named after other colors - Blanche, Olive, Viola, Pearl, Goldie - somehow don't readily become seductresses.] Even rose, which is but a pallid reminder of scarlet, manages to become tainted by the image of the lapsed woman [eg, Broadway Rose, Second Avenue Rose, Gypsy Rose Lee.] Red, in addition, has sometimes signified a sense of warning [eg, red traffic light] or ill-omen. Ancient Egyptian scribes switched to red ink when writing hieroglyphs announcing evil or wicked omens.

Still, none of these tangential observations serve to explain why Sydenham selected such a theologically sensitive hue as scarlet to define his infectious pharyngitis. For those concerned more with the biology of streptococcal infection than the historic baggage carried by certain colors, there is always Rhett Butler's immortal response to Scarlett O'Hara: "Frankly my dear, I don't give a damn!"

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Recent Advances in Cardiology

Daniel E. Forman, MD, Paul C. Gordon, MD, and Alfred F. Parisi, MD

MANAGEMENT OF HYPERCHOLESTEROLEMIA

Although an association between elevated plasma cholesterol and atherosclerosis has been known for many years, the benefits of cholesterol reduction remained controversial. Several recently completed randomized trials now clarify benefits of cholesterol lowering therapy for adults with known coronary artery disease (CAD).[1,2] Similarly, the just published West of Scotland Coronary Prevention Trial shows significant mortality and myocardial infarction benefit from primary cholesterol lowering therapy.[3]

ABBREVIATIONS USED

AF	Atrial fibrillation
AMI	Acute myocardial infarction
ATP	Adult treatment panel
AV	Atrioventricular
AVNRT	AV nodal re-entry tachycardia
BENESTENT	BElgium-NEtherlands STENT
BOAT	Balloon vs. Optimal Atherectomy Trial
CABG	Coronary artery bypass graft
CAD	Coronary artery disease
CAVEAT	Coronary Angioplasty vs. Excisional Atherectomy Trial
CCAIT	Canadian Coronary Atherosclerosis Intervention Trial
CCAT	Canadian Coronary Atherectomy Trial
CPK	Creatine phosphokinase
DC	Direct current
DCA	Directional Coronary Atherectomy
ECG/EKG	Electrocardiogram
ELCA	Excimer Laser Atherectomy
ERBAC	Excimer Rotational Balloon Angioplasty Comparison
GUSTO	Global Utilization of Streptokinase & Tissue Plasminogen Activator for Occluded Coronary Arteries
HARP	Harvard Atherosclerosis Reversibility Project
HDL	High density lipoprotein
HMG-CoA	3 hydroxy-3-methylglutaryL coenzyme A reductase
INR	International normalized ratio
LA	Left atrium
LBBB	Left bundle branch block
LDL	Low density lipoprotein
LV	Left ventricle
LVEF	Left ventricular ejection fraction
MAAS	Multicentre Anti-atheroma Study
NCEP	National Cholesterol Education Program
OARS	Optimal Atherectomy Restenosis Study
PAMI	Primary Angioplasty in Myocardial Infarction Trial
POSH	Program on the Surgical Control of Hyperlipidemias
SPAF	Stroke prevention in atrial fibrillation
4S	Scandinavian Simvastatin Survival Study
STRESS	STent REStensosis Study
SVG	Saphenous vein graft
TEC	Transluminal Extraction Atherectomy
TEE	Transesophageal echocardiography
TIA	Transient ischemic attack
tPA	Tissue plasminogin activator E

The largest *secondary* prevention trial, the Scandinavian Simvastatin Survival Study (4S), studied 4,444 angina pectoris or acute myocardial infarction patients aged 35-70 years for 5.4 years.[1] Initial total plasma cholesterol levels were between 212.7 and 309.4 mg/dl. Simvastatin reduced total cholesterol 25% and low density lipoprotein (LDL) cholesterol 35%; these reductions were associated with 42% fewer cardiac deaths and significantly lower stroke rates. Mortality-reduction extended to subjects with highest as well as modest baseline cholesterol elevations.[4] Mortality benefit also was found in 2,282 patients over age 60; there was no increase in non-coronary mortality in subjects with reduced cholesterol concentrations. The recently announced (ACC, 3/96) CARE Trial (Cholesterol and Recurrent Events) similarly showed 24% reduced fatal coronary heart disease and nonfatal MI among 4,159 Post-MI patients (mean total cholesterol of 209 mg/dl) who were treated with Pravastatin. Similar safety of cholesterol-lowering was evident in the recently reported follow-up from the Program On the Surgical Control of Hyperlipidemias (POSCH) trial, in which stable non-coronary mortality persisted during 12 years of lipid reduction after ileal bypass.[5]

Other recent trials have shown that statin drugs decrease atheromatous arterial obstruction. The Multicentre Antiatheroma Study (MAAS) was conducted over four years in 381 CAD patients with elevated cholesterol concentrations (245.6 ± 28.2 mg/dl).[2] Serial coronary angiograms showed less lesion progression (including fewer new lesions and total occlusions) and more lesion regression in the simvastatin cohort. In the Canadian Coronary Atherosclerosis Intervention Trial (CCAIT),[6] lovastatin therapy was associated with improved angiographic outcomes in 331 patients over two years. In the Regression Growth Evaluation Statin Study, pravastatin showed similar benefits in 884 CAD patients with milder hypercholesterolemia (232.8 ± 33.3 mg/dl) treated for two years.[7] Pravastatin and lovastatin also were effective in recent studies using carotid ultrasound to assess carotid vessels in asymptomatic hypercholesterolemic men and women.[8,9] The patients medicated with either drug had diminished intimal-medial carotid thickening; and in the lovastatin study, significantly improved clinical outcomes.[8]

Not all secondary prevention trials have shown *obvious* benefit of cholesterol reduction. The Harvard Atherosclerosis Reversibility Project (HARP) showed no angiographic benefit in patients with *normal* cholesterol concentrations (between 174.0 and 232.0 mg/dl) who received statin treatment for three years.[10] Still, the angiographic effects of cholesterol therapy may provide only partial assessment of possible therapeutic efficacy. While small degrees of regression are detected in some trials, reduction in new clinical events, such as death, recurrent myocardial infarction, and the need for coronary artery revascularization are often disproportionate to small gains in luminal diameter. Such benefits have lead to other investigations and evolving insights in the biology of vascular function and the related effects of cholesterol plaque.

Whereas atherosclerosis was once thought to clog arteries slowly and progressively, it is now evident that even small atherosclerotic lesions can produce clinical events depending on the composition of constituent lipids with related changes in the vasoresponsiveness in the coronary vessels. Lowering serum LDL concentrations stabilizes atherosclerotic plaque prone to ulceration and thrombosis and also restores normal endothelially mediated vasoresponsiveness, and hence greater resistance to myocardial ischemia.[11,12]

Given our evolving understanding of the benefits of cholesterol-lowering therapy, the results of the West of Scotland primary prevention trial are not surprising.[3] In this randomized placebo-controlled megatrial, 6,595 men aged 45 to 64 years were studied. They had mean hypercholesterol levels of 272 (23 mg/dl but no histories of myocardial infarction. After 4.9 years average follow-up, pravastatin (40 mg q hs) therapy was associated with 31% fewer nonfatal myocardial infarctions, 20% fewer deaths from coronary heart disease, and 32% fewer deaths from all cardiovascular causes. Furthermore, there was no excess of non-cardiovascular deaths associated with pravastatin therapy.

Recent advances in the management of hypercholesterolemia, atrial fibrillation, interventional coronary revascularization, primary angioplasty in myocardial infarction, radiofrequency ablation of arrhythmias and therapies for obstructive hypertrophic cardiomyopathy.

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Even before these prodigious 1994 and 1995 trials, more aggressive strategies for cholesterol management emerged. In June1993, The Second Adult Treatment Panel (ATP II) of the National Cholesterol Education Program (NCEP) released updated guidelines for the detection and treatment of hypercholesterolemia.[13] Recommendations are for cholesterol screening to be broadened to include *HDL as well as LDL* cholesterol levels. ATP II also mandates that cardiovascular risks, including age (males aged 45 years and females aged 55 years), family history of premature CAD, cigarette smoking, hypertension, low HDL cholesterol, and diabetes mellitus be factored in cholesterol-lowering therapeutic recommendations. An HDL cholesterol level ≥60 mg/dl also was recognized as a *negative* risk factor that may potentially modify the need to treat an elevated LDL cholesterol.

According to ATP II guidelines, adults aged 20 years without known atherosclerotic disease should have their total and HDL cholesterol levels checked every five years. For primary prevention, total cholesterol level is classified as desirable (<200 mg/dl), borderline high (200-239 mg/dl), or high (240 mg/dl). Patients with either 1) high total cholesterol, 2) borderline-high total cholesterol and two other risk factors, or 3) low HDL cholesterol (<35 mg/dl) should undergo fasting lipoprotein analysis to determine LDL cholesterol level. LDL cholesterol in primary prevention is classified as desirable (<130 mg/dl), borderline high (130-159 mg/dl), or high (160 mg/dl). If LDL cholesterol is high, or if it is borderline high and two other risk factors are present, dietary therapy with a Step One Diet (total fat intake <30% of calories/day, saturated fat 8-10% of calories/day, and dietary cholesterol <300 mg/day) or, if necessary, a Step Two Diet (saturated fat <7% of daily calories and cholesterol <200 mg/day) is initiated. Drug therapy is recommended if LDL cholesterol remains ≥190 mg/dl (or if LDL cholesterol is 160 mg/dl) and two other risk factors are present.

For secondary prevention in CAD patients, ATP II recommends a brief attempt with dietary therapy using a Step Two Diet (saturated fat <7% of daily calories and cholesterol <200 mg/day). Thereafter, if LDL cholesterol levels remain ≥ 130 mg/dl, drug therapy is recommended. The LDL cholesterol target is < 100 mg/dl.

The recently released American Heart Association consensus panel unequivocally indicates that lipid evaluation and therapy is integral to optimal care in cardiac patients.[14] Even secondary prevention for elderly adults is becoming less controversial. Due to the higher rates of infarction in older CAD patients, the absolute benefit of lipid-reduction is considered by some to be 4 to 18 times greater than in younger adults.[15] A growing body of literature on older coronary patients supports the benefits of risk factor modification, including exercise programs and cholesterol-lowering pharmacologic therapy.[15]

HMG-CoA reductase inhibitors (the statins) are now regarded as first line therapy in LDL hypercholesterolemia due to their established efficacy in reducing cardiac events and death in CAD patients. Moreover, they are well-tolerated in most adults. Despite their high cost, they are considered optimal therapy for most adults with elevated LDL cholesterol with an ultimately favorable cost-benefit ratio. Bile acid sequestrants are useful as secondary agents and can be effectively combined with statins in patients without high triglycerides. Statins and bile acid sequestrates are synergistic, and low-doses of each can be combined to yield maximal benefits with a minimum of side-effects. Fibric acid derivatives (gemfibrizol) remain useful, particularly in patients with high triglycerides. Short-acting niacin is also an effective and low-cost drug for elevated LDL cholesterol, with the added benefits of decreasing triglycerides and raising HDL. Niacin-related flushing effects are often reduced by prior aspirin administration. Estrogen also lowers plasma cholesterol. For post-menopausal women, the relative benefits of estrogen must be weighed relative to risks of uterine and breast cancer which also increase with estrogen therapy. The ongoing Women's Health Study promises to clarify whether estrogen therapy is advantageous, despite inherent risks for comorbid disease.

MANAGEMENT OF ATRIAL FIBRILLATION

Atrial fibrillation (AF) is the most common sustained arrhythmia. Its prevalence swells to almost 13% in adults aged over 70.[16] With loss of coordinated atrial contraction, cardiac output diminishes, impairing exercise tolerance particularly in older AF patients, and there is significant risk of thromboembolic events.

Initial treatment of AF depends on patient stability. Immediate direct current (DC) cardioversion is recommended for AF patients who have hypotension, angina, or left ventricular dysfunction with pulmonary edema.[17,18] For more stable AF patients, ventricular rate control is the initial therapeutic goal. Digitalis glycoside (digoxin) was once the primary therapy to achieve rate control by impeding AV nodal conduction. Digoxin dose is titrated upward until a slower heart rate is achieved, usually over a period of several hours. Such rate-limiting effects of digoxin, however, can be overwhelmed by a sufficient sympathetic stimulus, such as emotional stress, intercurrent illness, or exercise.[19] While the rate-controlling effects of digoxin may be augmented with still higher doses, the risk of digoxin toxicity also increases.

Given these limitations of digoxin therapy, alternative medications to slow AV conduction and ventricular rate have become popular. Beta-blockers or calcium channel blockers (verapamil or diltiazem) used alone or concurrently with digoxin can safely achieve more rapid and effective ventricular rate control.[20,21] However, these drugs are negative inotropes and should not be used in patients with severe ventricular dysfunction.

AF is present in 50% of patients with thromboembolic strokes.[22] Risk-factors for stroke in patients with non-rheumatic atrial fibrillation include a prior history of stroke or transient ischemic attack (TIA), diabetes mellitus, hypertension, congestive heart failure, angina, myocardial infarction, LV dysfunction, left atrial enlargement, mitral valvular calcification, and advanced age. The strongest risk factors are advanced age and history of previous stroke or TIA.[23]

In comparison with aspirin and placebo, multiple prospective randomized studies have demonstrated that AF patients treated with long-term oral warfarin sodium (Coumadin) anticoagulation have fewer strokes. A recent analysis of nonrheumatic AF trials led to several general recommendations:[23] 1) Patients younger than age 60 with lone AF have a low risk of stroke and do not need to be anticoagulated. 2) Patients aged 60 to 75 with lone AF have a 2% annual incidence of stroke. While anticoagulation for these patients remains controversial, many feel their risk of stroke risk is sufficient to warrant warfarin therapy. 3) Patients younger than age 75 with even one risk factor for stroke have considerable stroke risk, and therefore benefit from oral anticoagulation. 4) Patients older than age 75, even without other risk factors, benefit from warfarin therapy because of high risk of stroke associated with advanced age.

The risk of intracranial hemorrhage in patients receiving warfarin increases in patients older than age 70, especially if the international normalized ratio (INR) rises above 3.0.[24] Therefore, an INR of 2.0 to 3.0 is deemed optimal, and careful monitoring of the INR every 3 to 4 weeks is advised.[25] Patients who cannot take warfarin (e.g. patients with recent gastrointestinal bleeding, alcohol abuse, poor compliance, or frequent falls) can be treated with aspirin 80 to 325 mg once a day.[26] However, preliminary results from the SPAF 2 trial indicate that aspirin is significantly *less* effective than warfarin in the older age (>75) group.[27] Warfarin, therefore, remains the therapy of choice for all patients who can tolerate anticoagulation.

While rate control and anticoagulation are valuable strategies, AF patients benefit most from cardioversion to sinus rhythm. Cardioversion should be attempted at least once for AF patients. With successful restoration and maintenance of sinus rhythm exercise capacity is increased, the risk of stroke is reduced and the need for anticoagulation is eliminated.[17]

Several strategies exist for cardioversion. Electrical (DC) cardioversion is efficient, cost-effective, and safe with a success rate of 85%.[18] Prior to elective DC cardioversion, patients who have had AF for more than 3 days, or in whom the duration of AF is not known, should be orally anticoagulated to an INR of 2.0 to 3.0 for at least three weeks to decrease the risk of embolism.[28]

An alternative and newer strategy is to screen patients with *new onset* AF within two days using transesophageal echocardiography (TEE) immediately prior to cardioversion.[29,30] TEE allows imaging of thrombi in the atrial appendages and detects spontaneous LA contrast (smoke), both of which are associated with increased thromboembolic risk.[31,32] If TEE detects no clots or smoke, DC cardioversion can proceed safely. Whatever precardioversion strategy is employed, warfarin therapy should be maintained for 3 to 4 weeks *after* cardioversion since the atrium may not contract normally for several weeks after sinus rhythm is restored leaving patients temporarily predisposed to thromboembolic events.[33,34,35]

An alternate approach is pharmacological cardioversion. Oral quinidine has traditionally been used to convert AF to sinus rhythm. Other options are procainamide, and most recently sotalol and amiodarone. Conversion to sinus rhythm is achieved with 25 to 50% of patients treated with procainamide, quinidine, or sotalol HCl.[36] Because of the proarrhythmic effects of these agents, careful in-hospital ECG monitoring during the initiation of drug therapy is recommended to avoid excessive QT interval prolongation.

After cardioversion, three-fourths of patients revert to AF if not treated with antiarrhythmic agents.[37] Even in patients using quinidine and procainamide, only 50% remain in sinus rhythm 6 to 12 months after cardioversion.[38] Patients who have had AF less than 12 months are less likely to develop recurrence of the arrhythmia.

Sotalol and amiodarone also are beneficial in maintaining sinus rhythm after cardioversion. Sotalol has been shown to be as effective as quinidine.[39] Amiodarone has been shown to be more effective than quinidine.[38,40] Oral amiodarone in doses 200 to 400 mg/day maintains sinus rhythm in more than 60% of patients. Therefore, if a patient reverts to AF while receiving therapeutic doses of procainamide or quinidine, repeat cardioversion followed by amiodarone may maintain sinus rhythm. Both sotalol and amiodarone have the advantage of controlling the ventricular rate should AF recur.

Amiodarone increases the effects of warfarin and digoxin. Typically, doses of those drugs are reduced by 50% upon initiation of amiodarone, and patients should be additionally monitored with frequent INRs and ECGs to assess for toxic coumadin or digoxin effects. Amiodarone is associated with many toxic effects: e.g., pulmonary fibrosis or thyroid dysfunction, however the low doses (200 mg/day) are effective for AF patients and are better tolerated.[40] For those few patients who remain in AF with difficult to manage high ventricular response rates AV node ablation or modification by radiofrequency catheter techniques may be helpful (see below).

Advances in Interventional Coronary Revascularization

The number of percutaneous coronary interventions performed in the United States has grown to nearly 500,000 cases per year. Until 1990, balloon angioplasty was the only percutaneous modality available for treating stenotic coronary arteries. While current *success rates* approach 95%, balloon angioplasty continues to be limited by difficulty crossing and/or dilating certain lesions, especially chronic total occlusions and calcified lesions; difficulty dilating rigid (fibrotic or calcified) or "elastic" (eccentric or ostial) lesions; and acute vessel closure (due to dissection and/or thrombus formation). Moreover, the biggest "Achilles heel" of balloon angioplasty is restenosis within the first 3-6 months which results in recurrent angina and/or the clinical need for repeat revascularization in 20-30% of patients. Multiple studies using pharmacologic therapy to inhibit the neointimal smooth muscle proliferative response contributing to restenosis have all failed to show benefit.(41) Thus, several new devices for percutaneous coronary intervention have become available in attempts to overcome limitations to treat lesions unfavorable for balloon angioplasty, to decrease the incidence of acute vessel closure, and to achieve safely the largest post-treatment luminal diameter, which is the strongest predictor of long-term angiographic and clinical success following any percutaneous coronary intervention.[42]

Atherectomy refers to removal of atherosclerotic plaque rather than the mechanical displacement or compression caused by balloon angioplasty. Directional Coronary Atherectomy (DCA) using the *Simpson Atherocath*™ involves the use of a windowed steel housing which contains a rotating cup-shaped cutter used to excise plaque. Based on early reports that DCA could be safely and effectively performed, especially in eccentric lesions generally unfavorable for balloon angioplasty, the randomized CAVEAT (Coronary Angioplasty versus Excisional Atherectomy Trial) and CCAT (Canadian Coronary Atherectomy Trial) studies were conducted. These trials confirmed that atherectomy yielded larger post-treatment luminal diameters (2.0-2.3 mm for DCA vs. 1.8-2.1 mm for balloon angioplasty) and lower residual stenoses (25-29% vs. 33-36%) than balloon angioplasty, but there was no benefit in late angiographic restenosis or the need for repeat revascularization, at the expense of a slightly higher rate of non Q-wave myocardial infarctions and a slight increase in 1 year mortality in the atherectomy patients.[43,44,45] The main criticism of these two trials was that DCA was not performed aggressively enough. Tissue removal accounts for only one-half of the luminal gain with DCA, with the other half accounted for by mechanical dilatation due to the bulky nature of the 6 or 7 French DCA device. In addition, despite initial concern, the removal of deep wall components (media and adventitia) by atherectomy was found to be safe and produced larger post-treatment luminal gains. Balloon dilatation after DCA (not routinely allowed in CAVEAT or CCAT), has also been shown to safely and effectively increase the post-atherectomy treatment lumen.

Two ongoing trials -- the OARS (Optimal Atherectomy Restenosis Study) and randomized BOAT (Balloon versus Optimal Atherectomy Trial) -- have clearly shown that more aggressive tissue removal followed by adjunctive balloon dilatation (if necessary) results in larger post-treatment lumen diameters (2.8 mm compared with 2.0 to 2.3 mm seen in CAVEAT and CCAT) and lower residual stenoses (15% vs. 26-29% in CAVEAT and CCAT) without an increase in complications. Late follow-up from these trials is not yet available. Currently, DCA is the preferred approach for treating most non-calcified ostial or eccentric lesions, or bifurcation lesions in the proximal left anterior descending or circumflex arteries.

Rotational Coronary Atherectomy involves a diamond-chip (5-10 um diameter) coated metal burr driven at high speeds (160-200,000 RPM) as it is slowly advanced across a coronary stenosis over an angioplasty guidewire. Rotational Atherectomy produces *differential cutting* -- inelastic hard, calcific plaque is preferentially cut (whereas elastic tissue such as normal arterial wall is pushed away), with particulate debris (<5-10 um in diameter) being washed through the coronary circulation and removed by the reticulo-endothelial system. Transient slow distal flow caused by the particulate embolization associated with small CPK elevations are common consequences, but rarely have any long-term clinical significance. Ablation is followed by low pressure adjunctive balloon dilatation in nearly 80% of cases to maximize the post-treatment lumen diameter (smooth and further expand the vessel) and trials are currently underway to evaluate this strategy. Rotational atherectomy is more favorable for treating rigid, calcific, ostial, and long (>10 mm) lesions with higher success rates and fewer complications compared with convential balloon angioplasty but angiographic restenosis rates remain high (~38%).[46,47]

Transluminal Extraction Atherectomy (TEC) uses transcatheter suction to remove plaque and/or thrombi liberated by rotation of sharpened struts at the tip of the catheter. Used in less than 5% of interventions in labs where it is available, the device has been employed predominantly to remove thrombi from degenerated vein grafts and larger native vessels. In nearly all cases, it must be followed by conventional balloon angioplasty.

Excimer Laser Atherectomy (ELCA) involves photochemical ablation of plaque by high energy, ultraviolet (308 nm) laser pulses. Current laser catheters are small-sized (1.4-2.0 mm in diameter) and thus also require adjunctive balloon angioplasty in nearly all cases. With restenosis rates of approximately 50%; the ERBAC (Excimer Rotational Balloon Angioplasty Comparison) trial showed little benefit over rotational atherectomy in treating similar lesion morphologies; and with the high cost of the laser console -- excimer laser has not become widely available, and probably accounts for less than 5% of interventions in centers with the device.

Of all the new devices for coronary intervention, intracoronary stents have shown the greatest promise. Stents have been more successful than conventional balloon angioplasty techniques (i.e. long perfusion balloon inflations) at tacking-up severe dissections that contribute to acute vessel closure, leading to a lower incidence of myocardial infarction and need for emergency CABG. Stents also have an advantage over balloon angioplasty by providing an internal scaffold to prevent the 20-30% elastic recoil of the vessel wall seen immediately after conventional balloon angioplasty. Using serial intravascular ultrasound, it has been shown that restenosis following balloon angioplasty and atherectomy is equally attributable to adverse vessel *remodeling* (chronic recoil or vessel shrinkage that may be accounted for by peri-adventitial fibrosis and scar contraction) and *neointimal hyperplasia*.[48] Stents can provide a scaffold to prevent adverse late remodeling, and despite having more neointimal hyperplasia at follow-up than balloon angioplasty (due to increased deep subintimal injury), the net late luminal diameter after stenting will still be larger.

The randomized STRESS (STent REStenosis Study) and BENESTENT (BElgium-NEtherlands STENT) trials showed a 30% reduction in both angiographic restenosis and late repeat target vessel revascularization with stenting, compared with balloon angioplasty, accounted for solely by the larger post-treatment lumen diameter (2.5 mm vs. 2.0 mm) obtained with stenting, compared with balloon angioplasty. Unfortunately, despite the aggressive anticoagulation using peri-procedural dextran, intravenous heparin (until a therapeutic INR with coumadin was achieved), and Coumadin, aspirin and persantine for 4-8 weeks, there was still a 3.5% incidence of thrombotic subacute closure in the stent patients. The aggressive anticoagulation also resulted in a higher 7-13% incidence of combined vascular and major bleeding complications in the stent patients compared with 3-4% for the angioplasty patients, and the length of in-hospital stay was thus 3-5 days longer for stent patients.[49,50]

Since the results of the STRESS and BENESTENT trials, the technique of stent deployment has changed. High pressure balloon post-dilation to expand the stent optimally in apposition to the vessel wall (thus not allowing a nidus for thrombus to propagate) to achieve a 0-10% angiographic residual stenosis, or using intravascular ultrasound to confirm optimal, symmetric stent expansion and apposition, has led to markedly reduced anticoagulation regimens of aspirin alone or combinations of aspirin and ticlopidine with thrombotic subacute closure rates of 0 to <1% in several large series. In addition, the reduced anticoagulation regimen has led to reduced vascular and bleeding complication rates and hospital lengths of stay.[51]

PRIMARY ANGIOPLASTY IN MYOCARDIAL INFARCTION

Plaque fissuring within coronary arteries with the formation of overlying occlusive thrombus is widely recognized as the cause of the majority of cases of acute myocardial infarction (AMI). Randomized, placebo-controlled trials of thrombolytic therapy for evolving AMI have demonstrated that early reperfusion can salvage myocardium, improve left ventricular function, and reduce mortality. However, thrombolytic therapy fails to restore patency in 20-30% of arteries, and severe residual coronary stenoses are often present in those patients in whom it is successful. Thrombolysis also has significant risk of recurrent ischemia and reinfarction (25-35%) and of serious bleeding complications including intracerebral hemorrhage (0.5-1%). Furthermore, the majority of patients who present with AMI are not candidates for thrombolytic therapy. Thus, *primary* or *direct* angioplasty has been increasingly used as an alternative to thrombolytic therapy to restore vessel patency in AMI.

Extensive experience with primary angioplasty from several centers has been reported. In a meta-analysis of 10 studies including 2,073 patients by Eckman, et al. -- including patients with cardiogenic shock and those deemed ineligible for thrombolytic therapy -- infarct vessel patency was restored on average in 91% of patients. Combined in-hospital mortality was 8.3%, with a mortality of only 1% in patients with single vessel coronary artery disease.[52] The largest single-center experience originates from the Mid America Heart Institute; in 1,000 consecutive patients (with infarct vessel recanalization in 94% of patients), the 1 and 5 year survival rates were 95% and 84%.[53]

The Primary Angioplasty Registry prospectively involved 271 patients presenting within 12 hours of the onset of chest pain, excluding patients with cardiogenic shock and life-threatening anatomy (left main or severe 3 vessel CAD) needing coronary artery bypass graft surgery (CABG). *Reperfusion* was successful in 98%, with a less than 50% residual diameter stenosis obtained in 92% of patients. Urgent CABG was required in 5% -- 3 patients for failed angioplasty and 11 patients for life threatening anatomy. In-hospital mortality was 4%, reinfarction occurred in 3%, recurrent ischemia occurred in 10%, and stroke (1 hemorrhagic and 2 embolic) occurred in 1% of patients.[54] At 6 month follow-up, death occurred in 2%, reinfarction in 3%, and recurrent ischemia (with readmission for chest pain) in 10% of patients. Infarct vessel patency at 6 months was 87%; angiographic restenosis (defined as a >50% diameter stenosis) occurred in 45% of patients, resulting in repeat angioplasty in 20% of patients and CABG in 14% of patients.[55] Pooled data from other studies also confirms an average angiographic restenosis rate of 43% (range 32-52%), which is similar to restenosis following angioplasty for other indications.[56]

Three major trials have randomized patients presenting with AMI (with ST segment elevations and who had no contraindication to thrombolytic therapy) to either primary angioplasty or thrombolytic therapy. The Primary Angioplasty in Myocardial Infarction Trial (PAMI) randomized 395 patients to tPA or primary angioplasty, with principal endpoints being a composite of in-hospital death or recurrent non-fatal myocardial infarction and left ventricular ejection fraction at 6 weeks. Similar to the Primary Angioplasty Registry, 10% of patients were not candidates for PTCA, as 5% had coronary anatomy needing emergent CABG, and 5% did not require an angioplasty. Primary angioplasty was successful in 97% of patients; none needed an emergent CABG for a failed angioplasty. There was a trend toward lower in-hospital mortality in the angioplasty treated patients (6.5% in the tPA treated patients vs. 2.6% in the PTCA patients, $p=0.06$), but much of the mortality difference was accounted for by the 2% ($n=4$) intracranial hemorrhage (all of which were fatal) rate in the tPA treated patients. This was higher than the 0.7% intracranial hemorrhage rate reported in the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) Trial.[58] In hospital reinfarction occurred in 4.5% of tPA treated patients compared with 2.6% of PTCA patients ($p = 0.06$). The combined endpoint of death and reinfarction was significantly lower in the angioplasty treated patients (5.1%) compared with the tPA treated patients (12.0%, $p = 0.02$). In addition, in *high risk* patients defined as either age >70 years, presenting with an anterior myocardial infarction, or presenting with a heart rate >100 beats per minute, mortality was significantly lower in the angioplasty treated patients (2.0% vs 10.4%, $p = 0.01$). Recurrent ischemia occurred less frequently in angioplasty patients (10.3% vs 28.0%), and the duration of onset of chest pain to its resolution was shorter in the angioplasty treated patients (290 minutes vs. 354 minutes, $p = 0.004$). Neither left ventricular ejection fraction at rest (53%) nor exercise (56%) were different in the angioplasty or tPA-treated patients.[57]

The Mayo Clinic study randomized 108 patients presenting with AMI to either tPA or primary angioplasty, with the endpoint being the change in size of the perfusion defect between admission and discharge as assessed by the perfusion agent technetium-99m sestamibi. PTCA had a success rate of 96%. There was no difference in either the amount of myocardium at risk in the tPA or angioplasty-treated patients (31% vs. 27%), the final infarct size (15% vs 13% of the myocardium), or the amount of myocardial salvage (15% vs. 13%). There also was no difference in the left ventricular ejection fraction at discharge (50% vs. 53%) or 6 weeks in the lytic or angioplasty patients. The need for repeat revascularization for recurrent ischemia, however, was lower in the angioplasty patients (16%) compared with the tPA patients (36%).[59]

The Netherlands study randomized 142 patients presenting with AMI to either intravenous streptokinase or primary angioplasty. Endpoints included in-hospital recurrent ischemia, pre-discharge LVEF, and late angiographic infarct vessel patency. Sixty-five of the 70 patients randomized to PTCA underwent the procedure, with success in 64 patients. Three of the 5 patients not treated with angioplasty required emergency CABG surgery. Recurrent ischemia was more frequent in the lytic patients (38%) compared with the angioplasty patients (9%, $p < 0.001$) -- with unstable angina occurring in 19% versus 6% and recurrent myocardial infarction occurring in 13% of the lytic patients and none of the angioplasty patients. LVEF at discharge was higher in the angioplasty patients (51% vs. 45%, $p = 0.004$). Infarct vessel patency assessed an average 21 days later in the streptokinase group was 68% with a mean 76% residual diameter stenosis, whereas patency (assessed an average 42 days later) was 91% in the angioplasty group with a mean 36% residual diameter stenosis.[60]

The Netherlands study was extended to include a total of 301 randomized patients with primary angioplasty success in 97% of 152 patients randomized to that treatment. There was a 23% reduction in enzymatic infarct size with angioplasty compared to streptokinase, LVEF was 50% for angioplasty compared to 45% for streptokinase; most importantly, mortality in this larger group of patients was 2% in the angioplasty patients compared to 7.4% in streptokinase treated patients ($p = 0.024$).[61] As the size of each of the three originally reported randomized trials was too small to detect mortality differences as a primary endpoint, a subsequent meta-analysis of these confirmed a beneficial effect on mortality with primary angioplasty (2.2%) over thrombolytic therapy (5.8%, $p = 0.023$), with less non-fatal re-infarction (2.1% vs. 7.6%, $p = 0.0008$) in angioplasty treated patients.[62]

Primary angioplasty also has been studied in several different subgroups of patients. Typically, 50-60% of patients presenting with AMI are excluded from randomized trials, either due to contraindications to lytic therapy (i.e. bleeding risk or prior stroke), late presentations, or unqualifying EKG changes (LBBB, ST-depressions as opposed to ST-elevations). Reported success with primary angioplasty in these patients is > 93%. Mortality (5-10%) with primary angioplasty is slightly higher in these patients than for thrombolytic-eligible patients treated with primary angioplasty in the randomized trials, but it is lower than the 17% to 29% mortality seen for thrombolytic ineligible patients treated medically.[63]

Cardiogenic shock occurs in 7.5% of all AMI's, with an in-hospital mortality rate of nearly 80%. There has been no proven benefit in these patients with thrombolytic therapy, but survival in patients in cardiogenic shock treated with angioplasty is > 55%. Successful reperfusion can be established in more than 60% of patients, with survival > 70% in patients with angioplasty established reperfusion, but survival < 25% when angioplasty fails to establish reperfusion.

Elderly patients > 75 years of age with AMI have frequently been excluded from thrombolytic trials despite a 20-25% mortality. However, mortality remains approximately 15% even with thrombolytic therapy. Success rates for primary angioplasty in the elderly are > 90%, with reported mortality rates of 8-18%.

In patients with a prior history of a coronary artery bypass graft operation, the GUSTO Trial confirmed that mortality for AMI is increased (10.7% in patients with a prior CABG versus 6.4% in patients without a prior CABG). In addition, the infarct related artery was a saphenous vein graft in approximately 70% of patients.[58] Saphenous vein grafts notoriously have an increased thrombus burden which is resistant to lysis, with only a 25% reperfusion rate with thrombolytic therapy. In 130 consecutive patients reported form the Mid America Heart Institute Experience, the success rate for primary balloon angioplasty for AMI due to SVG occlusion was 86%.[53] The role of new devices in these patients such as Transluminal Extraction Atherectomy or Excimer Laser Atherectomy for primary intervention during AMI -- especially to avoid distal embolization of thrombus -- has not been well reported.

Thus, primary angioplasty clearly has improved patency rates for AMI patients (> 90%) compared with thrombolytic therapy (70-85%), and the total duration of chest pain is shorter, although the time to initial treatment onset is similar or may even favor thrombolytic therapy. The lower incidence of recurrent ischemia, re-infarction, and need for subsequent revascularization favors primary angioplasty. It has not been clearly shown that primary angioplasty improves myocardial salvage over thrombolytic therapy, but there does appear to be a trend toward improved mortality with primary angioplasty, particularly in "high risk" patients. Primary angioplasty also has a lower overall stroke risk, especially for intracranial hemorrhage which remains between 0.5 and 1% for thrombolytic therapy. Another potential advantage for primary angioplasty over lytic therapy may be lower costs, although costs were not shown to be significantly lower in the Mayo clinic study. Hospital lengths of stay usually are shorter for primary angioplasty, and there are fewer late in-hospital procedures such as nuclear stress testing or need for catheterization. The major limitation of primary angioplasty for AMI is that it is not widely available; only 18% of US hospitals have catheterization laboratories (and not all have angioplasty capability), and a dedicated call-team with experienced staff and physicians need to be available at all hours. In addition surgical back-up must be available as 5-10% of patients presenting with AMI who undergo cardiac catheterization may need emergent CABG surgery either due to life-threatening coronary artery disease not amenable to angioplasty or due to a failed angioplasty.

RADIOFREQUENCY ABLATION OF ARRHYTHMIAS

More than a decade ago, interest arose in abolishing arrhythmias by selective tissue damage to pathways needed for arrhythmia propagation. Initially, this was achieved with direct current (DC) catheter ablation. However, as a therapeutic method, DC ablation never received widespread support because it created excessive tissue destruction and required general anesthesia for its application. More recently, radiofrequencies have been applied through catheter tips to create focal tissue lesions by thermocoagulation of pathways responsible for arrhythmia propagation. Radiofrequency does not require general anesthesia for its application, produces very discrete lesions of the order of 5 mm or less and has been clearly proven to be safer than DC ablation. Radiofrequency energy usually in the range of 20-50 watts created from an electrosurgical unit is delivered through the tip of a steerable electrode catheter for 10-60 seconds. The operator can monitor the effectiveness of tissue contact either through measuring catheter tip impedance or temperature. As a result of its efficacy and safety, radiofrequency ablation has now become widely applied in most facilities that have electrophysiology testing laboratories.

Not all arrhythmias are suited for radiofrequency ablation. However, those arrhythmias that can be identified to depend on well-defined pathways often involving re-entry in or around the floor of the atrium or AV node are highly amenable to this technique. There has been widespread success in abolishing rhythms such as AV nodal re-entry tachycardia, atrio-ventricular re-entry (bypass tract) tachycardia, and more recent reports indicating that the technique can be used to abolish atrial flutter.[64] For occasional patients who have medically uncontrollable ventricular responses to atrial fibrillation, it has now been shown that by producing very selective damage to the posterior interatrial septum, the AV node can be modified so that rapid ventricular responses no longer occur with exercise in patients with atrial fibrillation, yet AV conduction is maintained.[65] Radiofrequency ablation technique has not been useful for treating most patients with ventricular arrhythmias. There are selected patients free of coronary disease, however, who do have ventricular arrhythmias susceptible to radiofrequency ablation. The most frequent of these have been located in the right ventricular outflow tract and in the posterior interventricular septum. To date, reports of abolition of AV nodal re-entry tachycardia (AVNRT) and atrio-ventricular (accessory pathway) tachycardias have been most frequently reported as successfully treated with catheter radiofrequency ablation. These are the most common forms of regular supraventricular tachycardias and are worthy of more comment.

The re-entry pathway for AVNRT does not fully lie within the discrete AV node but rather involves pathways in the surrounding perinodal tissues. In its usual form, there is a slow pathway allowing antegrade conduction from atrium to the ventricle with a fast pathway allowing re-entry from the ventricle to the atrium thus completing the re-entry circuit loop. Selective ablation, usually of the slow pathway, has a success rate in excess of 90% and also has minimum chance of AV block since the slow pathway is further removed from the discrete AV nodal tissue. Since 1991, multiple publications compiling experience in over 500 patients have shown the success of this technique in the hands of independent operators. If the slow pathway is the target of treatment, the incidence of AV block should be considerably less than 5%. The overall recurrence rate of the AV nodal re-entry tachycardia after successful initial treatment is approximately 5%. Patients with AVNRT who are difficult to control with medication should be seriously considered for this therapy.

Radiofrequency ablation has also been used with great success to abolish tachycardias that depend on an accessory pathway. The latter may be either manifest on the surface electrocardiogram as a δ-wave or it may be concealed. In the usual scenario, patients who have accessory pathways have orthodromic conduction through the AV node with retrograde conduction back to the atrium through an accessory pathway. Destruction of the accessory pathway through radio-frequency catheter ablation has been extremely successful with very low complication rates. With a total of over 1,500 patients treated in clinical reports from different laboratories all attesting to the high success (approaching 100%) and low complication rates when radiofrequency ablation of accessory pathways is attempted, it is clear that this is a therapy which should be considered as a first line option for *symptomatic* patients with atrioventricular re-entry tachycardia.

Patients with Wolff-Parkinson White syndrome who have a possible propensity to develop antegrade conduction through the accessory pathway should they develop atrial fibrillation, can do so at excessive (and life-threatening) ventricular response rates. For these patients, radiofrequency ablation should be considered the first line of therapy.

The use of radiofrequency ablation for other supraventricular and selected ventricular arrhythmias must be weighed carefully against the alternative therapeutic options. For most patients today with hemodynamically compromising ventricular arrhythmias, the use of implantable cardioverter defibrillators appears to be a more practical approach. However, for selected patients with well-defined pathways responsible for their ventricular tachycardia such as the right ventricular outflow tract, radiofrequency ablation can be a preferred mode of therapy. It is likely that with improvements in catheter technology and our understanding of arrhythmia pathways that the radiofrequency technique will come into even more widespread use in the future.

New Treatments for Patients with Obstructive Hypertrophic Cardiomyopathy

Patients with advanced forms of hypertrophic cardiomyopathy are prone to develop left ventricular outflow tract obstruction. This occurs because there is mid-systolic apposition of the mitral anterior leaflet at its chordal junctions with the interventricular septum. Obstruction occurs because of the prominence of the septum in the left ventricular outflow tract interacting with dynamic forces of flowing blood from the distal ventricle, which has the dual effect of both pushing the mitral apparatus into the outflow tract as well as creating a Venturi effect as blood leaves the ventricle further making it likely that the mitral leaflets will remain in the outflow tract in mid-systole. Patients who develop this obstructive phenomenon have an intraventricular systolic pressure gradient and often develop associated symptoms such as angina, syncope, and heart failure. Symptoms of heart failure, particularly exertional dyspnea, are very difficulty to manage. Negatively inotropic drugs have been advocated to treat this syndrome; however, their success rate has been low. Surgical myomectomy with removal of the obstructing tissue of the interventricular septum has been used as an alternative approach but its success has been limited to a few centers which have had great experience with the operation. Over the past two years, reports from the National Institutes of Health have indicated that patients with obstructive hypertrophic cardiomyopathy who are treated with dual chamber pacing achieve substantial symptomatic relief from symptoms of heart failure.[66]

Dual chamber pacing for treatment of obstructive hypertrophic cardiomyopathy appears to be beneficial for two reasons. First, by pacing the right ventricle one produces left bundle branch block and delays the timing of activation of the interventricular septal contraction, thus lessening the possibility for its maximum contraction in the left ventricular outflow tract during mid-systole. Secondly, by optimizing the atrioventricular pacing interval, one can also optimize left ventricular filling so as to allow less opportunity for obstruction during the subsequent phase of ventricular ejection in the next cardiac systole.

While the initial success of this technique has been reported in adults, more recent reports indicate that this technique can be applied to children. In five patients, mean age 12 years followed for more than six months after receiving dual chamber pacemaker implantation, Rishi and coworkers from Emory, reported significant left ventricular outflow gradient reduction as well as reduction in left ventricular mass and interventricular septal thickness. Currently, the group at the Mayo Clinic is conducting a randomized prospective study of dual chamber pacing for hypertrophic cardiomyopathy patients. Initial verbal reports from this group indicate that the technique is not a universally palliative procedure. However the encouraging results from the NIH and Emory may lead one to believe that in properly selected patients, dual chamber pacing offers significant symptomatic palliation.

A newer and more aggressive approach to treating LV outflow tract obstruction has appeared in England. Dr. Ulrich Sigwart recently reported non-surgical myocardial reduction of the hypertrophied interventricular septum by using alcohol injections into catheters that are selectively inserted into the first septal artery.[67] This technique produces local infarction of the obstructing interventricular septal tissue. In the first three patients so treated there was evidence of significant reduction in left ventricular outflow gradient and dramatic improvement in symptoms at least three months later. With the great present interest in interventional catheter techniques to treat cardiac lesions, this latter approach will likely receive great attention in the future as a possible method for treating this difficult to manage syndrome.

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Advances in Endrocrinology and Metabolism, 1990-1995

Charles B. Kahn, MD, and Preston Lamberton, MD

The last update of this subject was published in this journal five years ago. Thankfully, health system reform, managed care, the reduction in Medicare reimbursement for graduate medical education, and the ever increasing incursion of the insurance industry have not yet seriously affected clinical research and medical advances in this field.

Diabetes still repesents well over half of the various endocrine disorders that a clinician will see. Some very exciting and substantial advances have taken place during these past few years. Type I Insulin dependent diabetes mellitus (IDDM) has been well-established as an autoimmune disorder. The specific cellular antigen, glutamate decarboxylase (GAD) has been identified. It is of note that similar molecular biological techniques have identified the peroxidase enzyme in thyroid cells as the antigen for Hashimoto's thyroiditis and the 17-alpha hydroxylase enzyme in the adrenal cortical cells in idiopathic Addison's disease. It has been clear for some time that environmental triggers are also important in the actual development of Type I diabetes. Viruses remain very active candidates, and a bovine albumin peptide in cow's milk has also been identified.

ABBREVIATIONS USED

ACE	Angiotensin converting enzyme
AGE	Advanced glycoprotein end product(s)
BPH	Benign prostatic hypertrophy
CRH	Corticotrophin releasing hormone
CT	Computerized tomography
GAD	Glutamate decarboxylase
HDL	High density lipoprotein
IDDM	Insulin dependent diabetes mellitus
IgG	Immune G globulin
LDL	Low density lipoprotein
LHRH	Luteinizing hormone releasing hormone
LYSPRO	Lsypro insulin (lysine proline)
MIBG	3-methyliodobenzylguanidine
MODY	Maturity onset diabetes of the young
MRI	Magnetic resonance imaging
NIDDM	Non-insulin dependent diabetes mellitus
TSH	Thyroid stimulating hormone
VMA	Vanillylmandelic acid

Although in Type I diabetes the hereditary predisposition to the defect in the immune system remains poorly understood, genetic factors are more clearly identified as the basic etiologic contributor to Type II diabetes mellitus. Polymorphic chromosomal abnormalities to date have been identified but incompletely clarified. A subset of Type II diabetes is called maturity onset diabetes of the young (MODY). This is an autosomal dominant disorder, usually diet-controlled in younger patients. A mutation in the glucokinase gene has been identified and appears to be located on the long arm of chromosome 20.

Some new information has been uncovered in the pathogenesis of Type II non-insulin dependent diabetes mellitus (NIDDM). Exciting work has been ongoing on glucose transporters, which are glycoproteins, located in the cell membrane. *Glut 2* appears to be the glucose transporter in the beta cell and may be a significant factor in the beta cell's glucose sensing mechanism. *Glut 4*, an insulin sensitive glycoprotein, is the glucose transporter in skeletal muscle and adipose tissue. Defects in *Glut 4* are probably factors in the insulin resistance of Type II diabetes mellitus, primarily in skeletal muscle. In addition, deposition of an amyloid polypeptide in the beta cells has been noted with increasing frequency and may, or may not, be a factor in beta cell inertia and subsequent exhaustion. The amyloid polypeptide is apparently identical to the calcitonin gene-related peptide.

The most exciting development, a landmark study in diabetes, was the report of the Diabetes Control and Complication Trial. The data indicate that intensive treatment for Type I diabetes has the potential to reduce the prevalence of primary complications and/or stabilize or reduce early secondary complications between 50%-75%. A comparison of standard versus intensive treatment in Type II diabetes mellitus is in progress. A preliminary report is available and a final report may be available within the next three years.

Human insulin remains the standard for conventional or intensive insulin management. Concerns were raised in the literature about an increased likelihood of hypoglycemic unawareness with the human insulins. Further studies, however, failed to verify this phenomenon. A major advance recently has become available in the treatment of Type II diabetes mellitus. The FDA licensed the use of metformin (Glucophage). This is a biguanide with a basic structure similar to phenformin, an oral antidiabetic agent removed from the marketplace 17 years ago because of the risk of developing lactic acidosis. When used appropriately, metformin appears to be a much safer agent, with an extremely low incidence of lactic acidosis. The guidelines clearly indicate that metformin should not be given if there is any elevation in the serum creatinine. Of note is that metformin apparently does not cause hypoglycemia.*

A new analogue of regular insulin, human insulin (LYSPRO) has been developed by Eli Lilly and Company and is now undergoing clinical investigation. It is hoped that this will provide a form of regular, fast-acting insulin with a more predictable absorption time and duration of action than the presently available insulin.

Considerable work has been carried out in terms of evaluating and treating the end organ degenerative complications of diabetes mellitus. The value of angiotensin converting enzyme (ACE) inhibitors in early diabetic nephropathy appears to be well-established. A clinical guideline has been recommended concerning the need to evaluate patients for urinary microalbumin semiannually beginning with the first office visit for Type II diabetes and Type I diabetes mellitus after about ten years duration of disease. Aldose reductase inhibitors, i.e., alredase (Tolrestat), sorbinil (Pfizer), continue to be under study in the treatment of diabetic polyneuropathy. To date no agent has received FDA approval. Experience indicates that the clinical effect is limited and side effects substantial.

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*Acarbose (Precose) a new category of gastrointestinal disaccharidase inhibitors has just been released.

Amitriptyline (Elavil) has been used for some time in the treatment of symptomatic polyneuropathy. Other antidepressive agents have been shown to be effective such as desipramine (Norpramine) and trazodone (Desyrel). Erythromycin, initially intravenously and now orally, has been shown to be effective in some cases of diabetic gastroparesis. Cisapride (Propulsid), a prokinetic agent, has been added to metclopromide (Reglan) in the treatment of gastroparesis. An agent, aminoguanidine, still under investigation, appears to interfere with production of advanced glycoprotein end products (AGEs) These products are involved in many of the pathologic changes seen in the degenerative complications of diabetes mellitus such as thickened basement membrane substance which become an irreversible biochemical pathway.

Two other aspects of diabetes are worthy of mention. Attempts to interfere with the autoimmune process in the etiology of Type I diabetes mellitus continue. Cyclosporine was discussed in the last review. In the interim, nicotinamide, the B2 vitamin, has been shown to have immunomodulating properties and is presently under investigation. More recently, primarily in animal studies, insulin itself, during the period just prior to the development of clinical diabetes, has been shown to down-regulate the autoimmune process in the islets. A study is presently underway to identify first order relatives of Type I diabetic patients, survey them for the existence of the early autoimmune triggers, and expose such candidates to low-dose insulin therapy to see if the onset of disease can be modified.

The other area of continued interest is Syndrome X, also called the insulin resistance syndrome or the dysmetabolic syndrome. This syndrome is characterized by truncal (android) obesity, hypertension, dyslipidemia, predisposition to atherosclerosis, insulin resistance and glucose values within the normal range. Some recent data suggest the majority of patients with this syndrome have normal, albeit high normal, fasting glucose values between 105-115 mg/dl. Further clarification of the significance of this syndrome and the potential for various treatments are being considered.

> *A comprehensive review of recent advances principally in clinical diabetes mellitus, thyroid disorders, adrenocortical disease, calcium metabolism, estrogen and testosterone therapies and neuroendocrinological disorders.*

THYROID

After diabetes, thyroid disorders continue to be among the most common endocrine problems seen by physicians. One such common disorder is Graves' disease which produces hyperthyroidism via stimulation of the TSH receptor by IgG auto-antibodies. Like many autoimmune disorders, Graves' disease is often characterized by spontaneous relapses and remissions, likely due to the appearance or disappearance of the thyroid stimulating immunoglobulins. A widely cited study by a group of Japanese investigators has suggested that the addition of thyroxine to antithyroid medication methimazole (Tapazole) may dramatically improve the remission duration in patients with Graves' disease. When this study was first published in 1991, there was considerable interest and enthusiasm for this combination therapy. Unfortunately, there has not yet been confirmation that the addition of thyroxine to antithyroid drugs will improve the rate or duration of hyperthyroidism remission.

One of the more common diagnostic dilemmas faced by physicians evaluating thyroid function tests relates to the finding of a suppressed serum TSH level in patients with normal measurements of T_4 and T_3. It is quite clear that in patients with well documented hyperthyroidism, serum TSH levels are typically suppressed and measure well below the normal range with the current TSH assays. These hyperthyroid patients will characteristically have elevation(s) of circulating thyroid hormone levels (i.e., T_4 and/or T_3). At times, however, physicians will note that hospitalized or chronically ill patients will have suppressed TSH levels in the setting of normal thyroid hormone levels. In a study of older patients with isolated suppressed TSH levels, it has been found that most elderly patients with low TSH values are not thyrotoxic. It is likely, therefore, that other factors besides thyroid hormone levels are suppressing TSH secretion in such patients. Although it does seem likely that many patients with suppressed TSH measurements and normal thyroid hormone levels are not hyperthyroid, Sawin and colleagues demonstrated more recently that older patients with suppressed TSH values had a threefold higher risk of developing atrial fibrillation over time compared to patients with normal TSH levels. The implication is that the atrial fibrillation was a manifestation of hyperthyroidism in these patients. This study suggests that the physician should evaluate patients with suppressed TSH levels and normal thyroid hormone levels for any clinical evidence of hyperthyroidism and then follow carefully for the development of possible thyrotoxic signs and symptoms. At this time, however, it is not clear that such patients should be treated with antithyroid medications unless they develop some elevation of either total or free T_4 or T_3 levels.

Hypothyroidism is also most commonly due to autoimmune disruption of normal thyroid function. It has usually been thought that the development of primary hypothyroidism due to thyroid autoantibodies is a permanent condition, usually necessitating thyroid hormone replacement for life. A study by Takasu et al demonstrated that some hypothyroid patients may have a disappearance of the TSH blocking antibodies, associated with an improvement of thyroid function and a return to a euthyroid state over time. At this juncture, however, it appears that such temporary hypothyroidism occurs in only a minority of patients with autoimmune hypothyroid disease. Therefore, if a decision is made to give such patients a trial off thyroid hormone replacement, careful, early reevaluation is quite important.

In the area of thyroid disease and thyroid hormone therapy, numerous studies over the past several years have investigated the possible relationship between thyroid hormone medications and the development of osteopenia, particularly in postmenopausal women. It has been known for quite some time that endogenous hyperthyroidism can be associated with both hypercalcemia (rarely) and reduced bone mineral density. A logical extension, therefore, was to question whether patients treated with thyroid hormone medications would be at similar risk for bone loss and possibly fractures. Initial studies, principally from the United States, suggested that women on thyroid hormone therapy may develop a reduction in bone density, seemingly as a consequence of "over treatment" with thyroid hormone medications.

More recent studies, however, have perhaps provided a better perspective on this concern. Greenspan and colleagues found that patients treated with thyroid hormone suppressive therapy who had normal free T_4 values and suppressed TSH values had a relatively small decrement in bone density, described as "clinically minimal" in their paper. Similarly, it has been found that bone loss occurs in postmenopausal women on thyroid hormone medications but not in postmenopausal patients taking estrogen replacement. This suggests, of course, that the greatest risk for the development of such osteopenia may occur in older, postmenopausal women who are also estrogen deficient. At this time, it appears prudent for the physician treating patients with thyroid hormone to attempt to maintain the TSH level in a non-suppressed range, unless such patients are being treated for a condition in which TSH suppression is likely beneficial (e.g., thyroid cancer). Finally, physicians should be aware of a clinically useful summary of suggested guidelines for the treatment of hyper - and hypothyroidism published in the *Journal of American Medicine* in March 1995.

ADRENAL

The newest advances in clinical adrenal cortical disease were primarily in the area of diagnosis. The 24-hour measurement of free urinary cortisol remains the most valuable tool in diagnosing hypercortisolism of any cause. The gold standard of low dose/high dose dexamethasone suppression remains useful but 50% suppression at either level has a significant number of false positives. In most pituitary-dependent Cushing's disorders, high dose dexamethasone decreases urinary cortisol by 90%. Careful study of the so-called "adrenal incidentaloma" has revealed subtle abnormalities in glucocorticoid production in a significant number of cases without Cushing's syndrome features. A new test to attempt to differentiate Cushing's syndrome from pseudo-Cushing's, primarily of psychiatric origin, involves the low dose oral dexamethasone suppression with corticotrophin releasing hormone (CRH) intravenously. This appears to help the differentiation when there is a lack of clinical features of Cushing's but where there is a failure to suppress cortisol with 1 mg of dexamethasone overnight. Considerable data have appeared in the literature over the past few years indicating the usefulness of CRH testing in Cushing's syndrome. A 7-hour dexamethasone infusion was described which appeared to have excellent separation of various hypercortisol disorders, but its application in clinical "cost effective" medicine with DRG criteria appears to be limited.

Although adrenal disorders are less common in general than several of the endocrine problems already discussed, consideration of adrenal dysfunction, particularly hypofunction, should remain in the differential diagnosis of many commonly encountered signs or symptoms. A recent study published by Soni et al for example demonstrated that acute adrenal insufficiency may be more common than previously suspected in patients presenting with septic shock. Although the authors suggested that all patients with septic shock be treated with stress doses of corticosteroids following a rapid Cortrosyn test for diagnosis, it seems premature at this point to make such a recommendation until studies are published demonstrating the value of such therapy in controlled investigations.

DIAGNOSTIC SCREENING

MRI/CT scanning continue to aid in distinguishing types of adrenal tumors and hyperplasia. NP_{59} has been used as a newer nuclear medicine imaging technique but lacks widespread application at the present time.

Recent information has indicated that the plasma aldosterone/ plasma renin activity ratio can be an excellent screen for primary hyperaldosteronism. An elevated ratio increases the suspicion of primary disease and warrants further investigation. Evaluation of the ratio before and after Captopril challenge can increase the diagnostic sensitivity. Further elucidation of licorice-induced hypokalemia or pseudo-hyperaldosteronism was reported in the literature. A chemical byproduct of licorice is glycyrrhetinic acid, which blocks the cortisone to cortisol shuttle via 11-beta hydroxysteroid dehydrogenase and causes the hypokalemia.

Pheochromocytoma continues to represent an uncommon but intriguing endocrine hypertensive disorder. Data show that 24-hour urinary epinephrine and norepinephrine levels or total metanephrines remain the best screening tests. Few data indicate that VMA measurements are an adequate test. Plasma total or free metanephrine levels have recently been reported to have diagnostic value. 3-methyliodobenzylguanidine (MIBG} is an experimental imaging tool to diagnose adrenal and extra-adrenal pheochromocytoma. Its clinical application has yet to be established. The radioactive isotope of this compound also has been used to a limited extent in treating metastatic pheochomoctyoma.

OSTEOPOROSIS

In the area of bone and calcium metabolism, osteoporosis continues to be quite difficult to treat, especially when advanced. There are, however, a number of encouraging studies that have been published over the last several years dealing with this difficult problem. It has been known for years that estrogen therapy represents perhaps the most effective treatment for postmenopausal osteoporosis. A study by Prince et al confirmed again the value of estrogen replacement when compared with calcium and exercise alone for slowing postmenopausal bone loss. A more recent article published in

March 1995 also demonstrated that estrogen benefits both women shortly after menopause and also later in life (past age 65). Transdermal estrogen is now fairly commonly used for estrogen replacement therapy and several studies have shown similar benefits on bone mass with transdermal estrogen as seen with orally administered estrogen.

An interesting study published in February 1995 showed that Tamoxifen had similar effects to estrogen in preserving bone mass in postmenopausal women. In addition, slow-release fluoride and intranasally administered calcitonin have been recently shown to be of potential benefit in osteoporosis therapy and perhaps better tolerated than previously studieg forms of the fluoride or calcitonin treatments. Finally, corticosteroid treated patients are clearly at risk for developing disabling osteopenia. More recent studies have suggested that perhaps calcitonin, calcitriol (1,25 Vitamin D), and intermittent cyclic etidronate, may be helpful in alleviating bone loss in patients treated with long-term corticosteroid therapy. Alendronate (Fosamax), a new diphosphonate, has recently been approved and released for the treatment of postmenopausal osteoporosis. This additional medication will likely prove very helpful in the long-term management of patients with moderate or advanced osteoporosis disease.

Hypercalcemia of malignancy remains a frequent cause of morbidity in patients with a variety of cancers. The search for newer, more effective agents to combat this difficult problem has continued with at least several recent publications adding to our list of potentially effective medications in this setting. For example, both intravenous gallium nitrate and intravenous pamidronate (a new diphosphanate similar to etidronate or Didronel) have been shown to be quite effective in many patients with hypercalcemia secondary to malignancy.

Reproductive Endocrinology

In the area of reproductive gonadal endocrinology, the potential benefits and risks of estrogen replacement in postmenopausal patients has continued to dominate much of the clinical reproductive endocrine literature. As already mentioned, it has long been established that postmenopausal estrogen therapy lessens both bone loss and fracture rates in older postmenopausal women. More recently the beneficial effects of estrogen therapy on cardiovascular mortality also have been defined and several studies have attempted to explain why estrogen may have a protective effect on the cardiovascular system. It has been shown, for example, that oral estrogen has a benefical effect on LDL and HDL cholesterol levels in postmenopausal women. Interestingly, low dose transdermal estrogen did not have a similar effect, a not so surprising observation given the reduced hepatic effects of transdermally administered estrogen. This, however, may be dose-related since higher dose transdermal estrogen has been shown in the past to have beneficial effects on LDL and HDL levels. In addition, an article published last year proposes another cardiovascular protective mechanism of estrogen, the promotion of coronary vascular vaso-dilatation.

Finally, in terms of studies on estrogen therapy risks, two reports published in the last 12 months, unfortunately, leave physicians with an unclear answer as to the relationship of estrogen therapy to the development of breast cancer. The earlier study published in JAMA in late 1994 suggested that estrogen therapy has been used without any identifiable adverse effects on the course of disease in patients with breast cancer. When this study appeared, one was tempted to reconsider the prior clinical rule of thumb which considered a breast cancer history as a contraindication to estrogen replacement therapy.

The Nurses Health Study appeared in June of 1995 in the *New England Journal of Medicine* and re-suggested that the risk of breast cancer increased substantially among women who took estrogen replacement postmenopausally. And yet a few months later, still another large-scale study showed little risk. Clearly this difficult question regarding estrogen use and breast cancer remains a concern and must be considered a potential risk weighed against potential benefits in women considering postmenopausal estrogen therapy. At this time, however, it still appears very likely that for many postmenopausal women, the benefits of estrogen on menopausal symptoms, osteopenia, and cardiovascular mortality will outweigh the risks of estrogen therapy, including the concern about breast cancer. The risk-benefit analysis of estrogen replacement therapy is part of the ongoing Womens' Health Initiative.

The transdermal delivery of testosterone has been shown to be an effective therapeutic measure and can produce physiologic concentrations of testosterone and its metabolites in hypogonadal men. A variety of new measures have become available for the endocrine treatment and/or manipulation of benign prostatic hypertrophy. Finasteride, a $_5$-alpha reductase inhibitor, is now being used in the treatment of BPH.

Neuroendocrinology

In the area of neuroendocrinology, several recent studies have examined the possible incidence of occult pituitary adenomas in healthy adult patients and also the natural history of these benign tumors. It has been recently found that perhaps 10% of the normal adult population may harbor "asymptomatic" pituitary adenomas, as detected by MRI scanning. An important follow-up study would be to investigate the natural history of such lesions discovered incidentally when MRI scans are done for non-endocrine indications. In that regard, a study published in January of 1995 served to reassure physicians that pituitary "incidentalomas" may follow a benign course and, therefore, do not necessarily represent an indication for treatment when discovered. Such patients, however, should be studied with an extensive endocrine evaluation to look for pituitary dysfunction (hypopituitarism or hyperpituitarism, such as with Cushing's disease). Evaluation of these same patients also should include visual field testing since any significant visual field change would require consideration of therapy to reduce the size of the adenoma. Finally, a recent study by Constine et al has confirmed the concern about the potential development of hypopituitarism after irradiation therapy for brain tumors. Physicians following such patients need to periodically undertake a battery of pituitary function studies, especially with the development of any signs or symptoms that would be consistent with pituitary hypofunction.

MISCELLANEOUS

Evaluation and treatment of dyslipidemia remain an active area in endocrinology and metabolism. Much work has been carried out indicating that LDL must be oxidized, and in the oxidized form can apparently play a role in activating the atherogenic process. Of note in the therapeutic armamentaria has been the finding that phenolic substances found in red wine, garlic, the vitamin antioxidants, monosaturated fatty acids and estrogen therapy can reduce the oxidation of LDL and, therefore, potentially interfere with the atherogenic process. The ability to elevate HDL cholesterol remains difficult. Data continue to show that exercise is the best mechanism, although wine, particularly red wine, appears to have some beneficial properties.

Work in the field of obesity has shown that truncal or android obesity (high waist to hip ratio) is a much greater cardiovascular health hazard than pelvic girdle (gynecoid) obesity. Twin studies involving those reared separately or together suggest that genetic factors are far more important than environmental factors. Weight loss programs appear to have a preferential loss of the central obesity over pelvic girdle obesity, and this enhances the value of weight loss in reducing cardiovascular risk. It also has been found that weight loss followed by weight gain, so-called weight cycling, does not adversely affect cardiovascular risk.

Some advances also have been developed in pediatric endocrinology. Specific gene mutations and/or deletions have been found for several pediatric disorders. The growth hormone receptor gene mutation for the laron dwarf syndrome was discovered, as well as a deletion of the KAL gene in Kallmann's syndrome.

Considerable work has been recently done studying secretory growth patterns in constitutionally delayed growth and in other endocrine related short stature syndromes. The value of growth hormone treatment was well identified. In addition, an LHRH antagonist, deslorelin, improved the height in patients with precocious puberty.

The experience with near total thyroidectomy and radioactive iodine treatment in adult, differentiated thyroid carcinoma is well established. Such therapies have been studied in children and adolescents with differentiated thyroid cancer, and they appear to do equally as well as adults with no increased risk, in spite of their younger age. Finally, data are available indicating that calcium intake in adolescents is considerably below nutritional recommendations, and that there is evidence of higher frequency of age adjusted reduced bone mineral density in adolescent females. The recommendation of at least 1800 mg calcium per day is necessary as prophylaxis against late adult onset osteoporosis.

In conclusion, the authors of this review have selected articles covering the span from 1991 to 1995 that, in our opinion, have changed or will change the way physicians care for patients with endocrine disorders. Clearly, the explosion of new knowledge and technology that allows the identification of genes responsible for many non-endocrine diseases with the potential for the use of gene therapy in such conditions also will eventually affect the area of endocrine and metabolic diseases. For example, in an August 1995 issue of the *New England Journal of Medicine*, a study was published describing the importance of the beta-$_3$-adrenergic receptor gene in the pathogenesis of non-insulin dependent diabetes mellitus and morbid obesity. It is anticipated, therefore, that the next review may be devoted in part to the use of genetic testing and gene therapy in many conditions described in the current update on endocrinology and metabolism.

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Update of HIV and AIDS in North America

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EPIDEMIOLOGY AND TRANSMISSION OF HIV

Since 1981, when AIDS was first described as a clinical illness, it has become the leading cause of death of men and women between the ages of 25 and 44 in the United States.[1] Its incidence has plateaued among gay men in general since 1991, but continues to rise in African-American and Hispanic gay men. The greatest increase, though, in the shifting epidemic of AIDS in the United States, has occurred among injection drug users, women, and in particular, persons who have acquired HIV through heterosexual transmission. During the time when the documented number of cases of AIDS in the U.S. doubled from 100,000 to 200,000, HIV infection increased 20% in injection drug users, 30% in women, and 40% among persons with heterosexual transmission.

As with many sexually transmitted diseases, HIV infection is more efficiently transmitted to women than to men. Increased risk may be associated with a greater area of epithelium at risk of exposure in the female genital tract. Inconsistent condom use, genital tract infections (in particular, genital ulcerative disease), and noncircumcision in men have all been associated with a higher likelihood of HIV transmission. Unprotected anal intercourse is also associated with a greater transmission rate to recipient. It is encouraging to note, however, that in a European study of discordant couples, no seroconversions occurred in 124 couples consistently using condoms over two years.[2] Consistent condom use by persons at risk appears to be the most important factor in preventing continued sexual transmission.

ABBREVIATIONS USED

ACTG	AIDS Clinical Trials Group
AIDS	Acquired immunodeficiency syndrome
AZT	Zidovudine
bDNA	Branched deoxyribonucleic acid
BID	Bis in die [twice a day]
CDC	Centers for Disease Control
CMV	Cytomegalovirus
ddC	Zalcitabine
ddI	Didanosine
d4T	Stavudine
HIV	Human immunodeficiency virus
INH	Isoniazid
I V	Intravenous
MAC	*Mycobacterium avium* complex
PCP	*Pneumocystis carini* pneumonia
PPD	Purified protein derivative
PO	Per os
PCR	Polymerase chain reaction
RNA	Ribonucleic acid
ZDV	Zidovudine

Cocaine use in the United States is strongly associated with HIV transmission.[3] Crack cocaine is not injected, but its use often leads to overt prostitution, the exchange of sex for drugs, and increased high-risk sexual behaviors. Among women in New York City who used crack cocaine, the incidence of HIV infection was 4% per year, which is similar to that seen among U.S. gay men who have repeated unprotected anal intercourse.

Among HIV-infected women who are pregnant, the risk of transmission of HIV to the child is 25% - 30%. Increase in maternal-child transmission has been associated with advanced degrees of immunosuppression, low CD4 cell count, decreased CD4:CD8 ratio, p24 antigenemia, and high titers of viral load in the mother. Interruption of maternal-infant transmission of HIV was conclusively demonstrated by the single most impressive clinical trial conducted in any population of HIV-infected persons. AIDS Clinical Trial Group 076 documented that zidovudine (ZDV, AZT) could diminish transmission of virus from infected women to the newborn infants by over 67%.[4] Women were eligible to enroll in ACTG 076 if they were between 14 and 34 weeks of gestation, had a CD4 count >200, and had not previously received AZT therapy. Investigators at 59 sites in the U.S. and France enrolled 477 women. Women enrolled in ACTG 076 received AZT 100 mg five times a day before delivery, IV AZT in the intrapartum period, and the newborn infant received AZT elixir every six hours for six weeks after birth. The interim data from ACTG 076 demonstrated a remarkable reduction in acquisition of HIV for babies born of mothers who received AZT (13 infected infants, 8.3%) compared to mothers who received placebo (40 infected infants, 25.5%). The administration of AZT appeared to be safe for both mothers and infants. AZT treatment was not associated with prematurity or difference in infant length, weight, or head circumference at birth. Retrospective studies of HIV-infected women receiving AZT during pregnancy in New York and North Carolina supports the protective role of AZT in the prenatal period. The two-thirds reduction in vertical transmission appears most likely to be due to the use of AZT in the period before birth rather than the peripartum or postpartum period.

Studies are currently under way to determine whether women who have had prior experience with AZT will derive the same benefit from therapy as AZT-naive patients. At this time, there is nothing to suggest that women will not derive some benefit, and there is absolutely no evidence that AZT therapy would be harmful, even in women who are AZT-experienced. Studies using combination antiretroviral therapy and non-nucleoside antiretroviral therapy are now being planned to determine if additional benefit may be derived to prevent vertical transmission.

A major challenge for clinicians is to identify women who are infected with HIV and to link them with primary comprehensive care. In a recent study by the Centers for Disease Control (CDC) in rural Florida, 5% of 1,050 pregnant women were found to be HIV-infected.[5] Fully one-third of these women did not consider themselves to be at any risk of HIV infection; they had fewer than five lifetime partners, had never injected drugs, had never had a sexually transmitted disease, and had never had a sexual partner with known

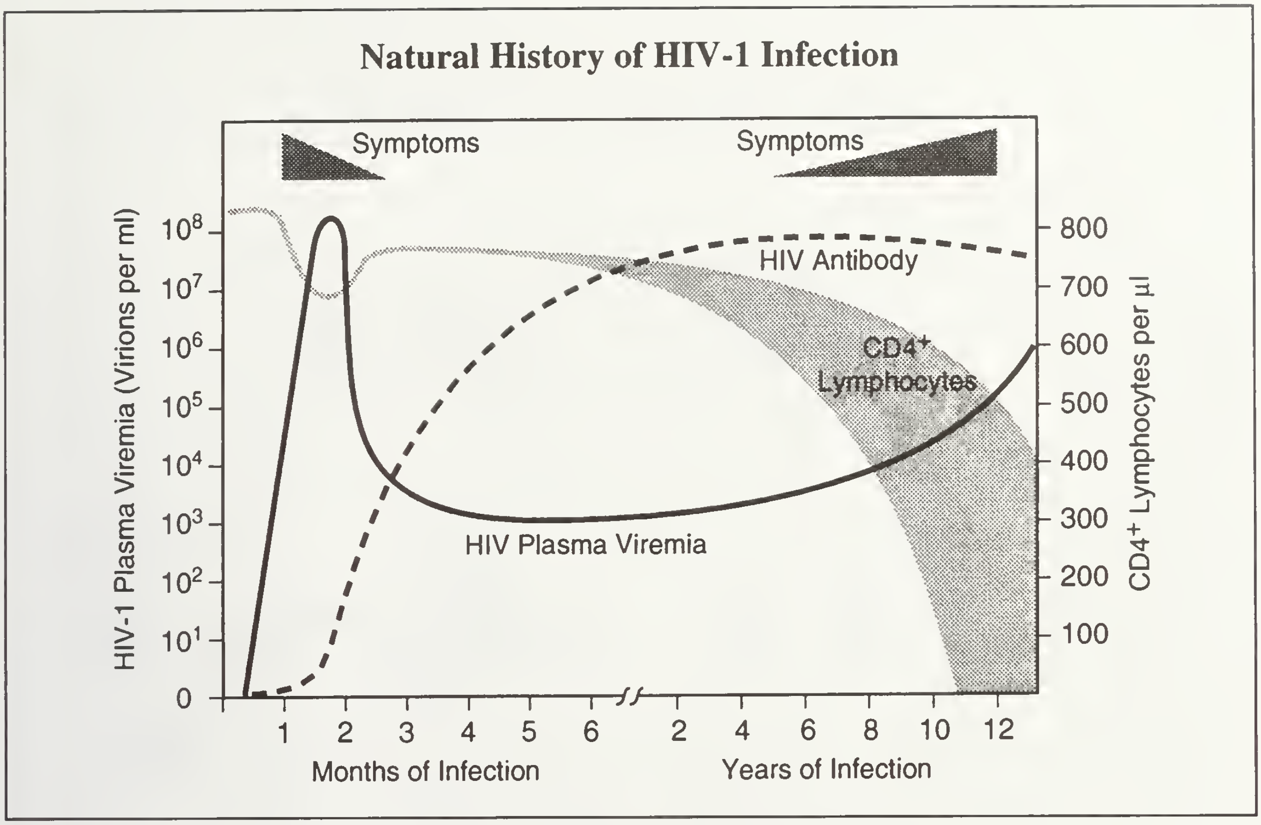
Natural History of HIV-1 Infection

Figure 1.

HIV. In multiple studies, HIV screening and counseling based on perceived risk has failed to detect 30-50% of seropositive women. Serial monogamy is accepted among many unmarried adults. Intercourse clearly places women at risk of acquiring HIV infection. It is therefore ineffective and inappropriate for health care providers to attempt to assess an individual woman's potential risk factors and then to offer only selective counseling and testing based on perceived risk. Data from North Carolina, Baltimore, and New York demonstrate that when counseling and testing are offered uniformly, over 3/4 of women in prenatal care will accept both counseling and HIV testing.

Pregnancy brings expectant mothers into contact with the health care system at an age when they are not routinely seeking medical attention. Because there is no comparable situation for men of the same age, universal counseling and voluntary HIV testing of pregnant women provides an appropriate opportunity to reach out and educate both pregnant women and their regular sexual partners. Since over 50% of HIV-infected women will be unaware of their infection, and because effective intervention now exists to prevent further transmission, it is imperative that *all* pregnant women be routinely offered compassionate, effective counseling and HIV testing.

HIV Pathogenesis and Viral Load

The acute phase of HIV infection (primary infection) is characterized by very high levels of HIV virus within the blood.[6] Approximately 50% of individuals are symptomatic, with a flu-like illness which frequently presents with fever, rash, pharyngitis, and lymphadenopathy. During acute seroconversion, characterized by the development of HIV specific antibody, an effective immune response develops which results in a dramatic fall in plasma viremia. Recent evidence suggests that HIV specific immune reactions mediated by CD8 positive lymphocytes are major components of recognition and down regulation of viral replication during this period.[7]

After acute seroconversion, individuals develop a clinically asymptomatic period. The duration of asymptomatic illness varies widely among infected persons and this variability appears to be due to both virological and immunological characteristics. In approximately 10% of infected persons, AIDS will develop within four years (rapid progressors).[8] Over 50% of persons will develop clinical manifestations of AIDS within ten years. Approximately 5% of patients will remain asymptomatic with normal CD4 cells for over ten years (long term nonprogressors). The variability in disease progression is important to consider when utilizing antiretroviral therapy. (Figure 1)

During the early phase of the epidemic, the rates of progression of HIV infection and survival were reported to differ among sociodemographic groups. It was unclear whether these differences were the result of access to primary medical care or biological variation. Recent data from over 1,500 patients followed at Johns Hopkins University indicate that when access to primary medical care is uniform, there is no difference in disease progression or survival associated with gender, race, injection drug use, or socioeconomic status.[9,10]

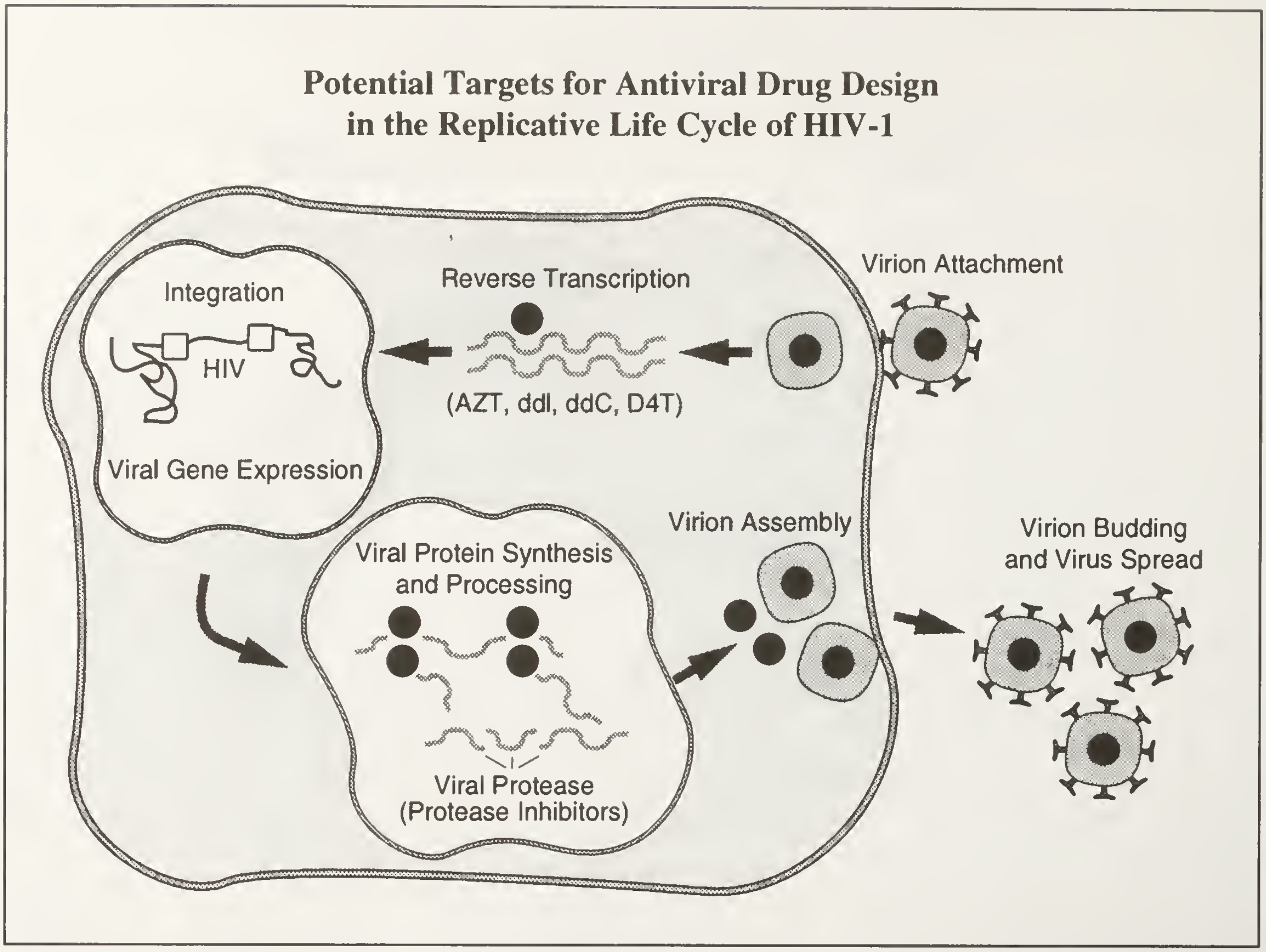
Potential Targets for Antiviral Drug Design in the Replicative Life Cycle of HIV-1

Figure 2.

It was previously believed that HIV was "latent" during the asymptomatic phase of infection. It is now possible to directly measure HIV replication through RNA quantification utilizing several assays; the level of ongoing viral replication is actually very high during the period of clinical latency. Quantitative polymerase chain reaction (PCR) and branched chain DNA (bDNA) assays have demonstrated that significant viremia persists after initial downregulation of virus.[11] During the asymptomatic phase of infection, viral replication is more active within lymph nodes than in blood. Immunohistochemical studies of lymph nodes of persons with early asymptomatic infection demonstrate replicating virus and intense immunological reactions within the lymph tissues.[12] As the disease progresses, the level of viral replication increases and eventually the lymph node architecture is destroyed. At that time, the level of replicating virus within the blood increases significantly. (Figure 2)

Studies which measured HIV viral load during antiretroviral therapy indicate that the half-life of HIV within plasma is very short (approximately two days).[11] This very rapid turnover of HIV indicates that nearly all the virus within the plasma has been produced by recently infected cells. Likewise, several studies indicate that there is a turnover of greater than 1 x 10^9 CD4 cells per day. HIV infection, therefore, is a dynamic process characterized by continuous rounds of viral infection, replication, and rapid cell turnover.

The finding that viral replication is high at all stages of disease presents a strong rationale for the benefit of early antiviral treatment. Early in the course of disease, there is a relatively homogeneous population of HIV which is likely to be more sensitive to treatment. As the disease progresses, high viral replication and the rapid rate of mutation of HIV generate a wide variety of variants that are more likely to lead to drug-resistant strains.

A preliminary study of AZT treatment during the acute phase of infection when the viral load is high indicated that patients treated with AZT for six months had a sustained stabilization of CD4 counts over eighteen months of follow-up.[13] On the other hand, both European and U.S. studies have demonstrated that AZT monotherapy in asymptomatic individuals with CD4 counts over 500 does not result in any clinical benefit.

Traditionally, the CD4 count within the blood has been used to follow the progression of disease and to determine when to begin or alter antiretroviral therapy. The ability to directly measure viral load through PCR or bDNA may lead to a more sensitive indicator of disease progression. There is a significant correlation between an increase in viral load and decrease in CD4 count. Among patients very early in the course of disease, a high viral load predicts more rapid progression to AIDS.[14]

Theoretically, measurement of viral load can be used in concert with CD4 cell counts to guide clinical therapy. Viral load results can be obtained rapidly, and appear to be relatively consistent over brief periods of time. Therefore, baseline and serial viral load tests could be used to assess the effectiveness of therapy.[15] For example, initiating AZT or ddI induces a rapid decrease in circulating HIV RNA by approximately fivefold. As HIV viral resistance emerges, the level of replicating virus increases and therapy can be altered. Ongoing clinical trials are assessing the ability of plasma HIV RNA quantification to successfully guide antiretroviral treatment.

With the high rate of HIV mutation, it is not surprising that development of resistance to antiretroviral agents is the rule rather than the exception.[15] Drug resistant strains of HIV emerge relatively quickly during antiretroviral monotherapy. These drugs do not induce the mutations, but they confer selective advantage on rare drug resistant sub-populations that are already present. Clearly, the Achilles' heel in antiretroviral therapy is the development of HIV viral resistance.

Using combination therapy with agents that inhibit viral replication at different points in the life cycle may inhibit the development of viral resistance and lead to more prolonged HIV suppression. A new class of drugs called protease inhibitors are currently under development; these drugs have a high antiviral potency, a favorable toxicity profile, and inhibit the HIV virus at a different stage than the nucleoside analogues, so that they are excellent candidates for multi-combination therapy. Currently, at least ten HIV protease inhibitors are in clinical trials or ready to enter clinical development. Three of these are likely to be available before this article goes to press. As a class, the protease inhibitors are active *in vitro* against HIV at nanomolar concentrations as compared to reverse transcriptase inhibitors (such as AZT, ddI, ddC, and D4T), which are generally active at micromolar concentrations. The protease inhibitors also are effective in both acutely and chronically infected cells such as macrophages, which are considered a major reservoir of HIV. The protease inhibitors have been tested in combination with AZT and ddC. The triple combination was associated with a significantly greater reduction of viral load and increase in CD4 count than either AZT or AZT plus ddC. The toxicity of the triple therapy was not significantly greater than monotherapy.

> *Better understanding of HIV pathogenesis, disease progression, antiviral therapy and opportunistic infection prophylaxis are leading to more effective therapy and prevention.*

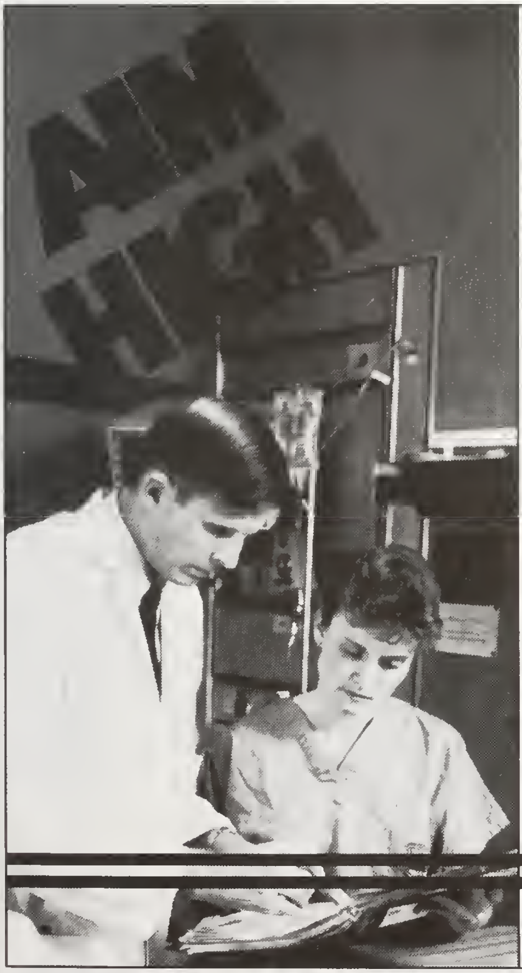

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Table 1
Initial Evaluation of Measures to Prevent Opportunistic Infections (OIs) in HIV-infected Adults and Adolescents

(1) Obtain a complete medical history, with emphasis on OIs.
- Constitutional symptoms, fever, weight loss
- Mucocutaneous candidiasis
- Pulmonary, gastrointestinal
- Positive TB skin test result, data and results of last TB skin test, history of treatment with antituberculosis drugs
- STDs
- Abnormal cervical Pap smear, date and results of last Pap smear

(2) Identify HIV risk behavior and assess ongoing high-risk behavior as well as other behaviors, activities, and interests that place patient at risk for TB and other infections.

(3) Perform physical examination directed by history but including genital and rectal examination for signs of STDs and (for women) routine gynecologic examination.

(4) Conduct laboratory and other tests.
- Complete blood count
- CD4+ lymphocyte count
- Blood chemistry profile and liver function tests
- IgG antibody to *Toxoplasma gondii*
- Antibody to CMV (if patient is not at such high risk for CMV that seropositivity can be assumed)
- Screening for STDs (RPR or VDRL, HbsAg, and anti-HBc), wet mount for trichomonas and bacterial vaginosis with possible testing for gonorrhea and (in women) for genital chlamydia infection
- Cervical Pap smear
- TB skin test (if result is not already known to be positive)
- Chest radiograph

(5) Initiate prophylaxis for PCP if patient has reliable history of CD4 count <200 (or 14.9%), PCP or thrush.

(6) Consider administration of pneumococcal vaccine if it has not already been given.

(7) Discuss need for future visits.
- Emphasis on the importance of OIs
- Emphasis on the importance of obtaining CD4 lymphocyte counts at appropriate intervals to determine timing/need for prophylactic interventions and antiretroviral therapy.

NOTE: Anti-HBc = antibody to hepatitis B core antigen; CMV = cytomegalovirus; HbsAg = hepatitis B surface antigen; PCP = Pneumocystis carinii pneumonia;RPR = rapid plasma reagin; STDs = sexually transmitted diseases; VDRL =Venereal Diseases Research Laboratory.

FROM: USPHS/IDSA Guidelines, CID 1995, 21:5 (supplement)

Evaluation of measures to prevent opportunistic infections

Routine Follow-up Care

- Directed history and physical examination
- Laboratory and/or other tests
  - Complete blood count, $CD4^+$ lymphocyte count, blood chemistry (as indicated)
  - Repeat TB skin test annually[a]
  - Repeat Pap smear[B]
- Chemoprophylaxis and vaccination
  - PCP if history of PCP, thrush, or fever of ≥ 2 weeks
  - Tuberculosis if positive TB skin test[c,d]
  - Suppress HSV recurrences as recommended
  - Hepatitis B vaccination if negative for antibody to HBc
- Behavioral advice
  - Sexual
  - Environmental / occupational
  - Pets
  - Food and water
  - Travel

↕

$CD4^+$ lymphocyte count <200/ul
- Prophylaxis against PCP

↕

$CD4^+$ lymphocyte count <100/ul
- Prophylaxis against toxoplasomosis if positive for antibodies to *Toxoplasma*

↕

$CD4^+$ lymphocyte count <75/ul
- Consider Prophylaxis against disseminated MAC[d]

HBc + hepatitis B core antigen; MAC = *Mycobacterium avium* complex; PCP = *Pneumocystis carinii* pneumonia: [a]Although reliability of the TB skin test may diminish as the CD4+ lymphocyte count deceases, repeat the TB skin test at least annually, depending on the risk of exposure to tuberculosis.[b]After an initialed negative Pap smear, repeat the Pap smear within 6 months. Thereafter, repeat the Pap smear annually.[c]Patients exposed to an active case of tuberculosis should also receive prophylaxis: those from populations at high risk for tuberculosis(i.e., a prevalence of >10%) may also be candidates for prophylaxis.[d]Exclude active mycobacterial disease before initiating prophylaxis.

Resistance will eventually arise with all effective protease inhibitors, although it appears to be delayed by combination therapy. Combination therapy with nucleoside analogues (AZT plus ddI or AZT plus ddC) is associated with greater magnitude and duration of immunological and virological benefit than monotherapy. The efficacy of AZT is also strongly enhanced by the addition of a new nucleoside analog, 3TC (Lamivudine), which appears to inhibit HIV resistance to AZT.

OPPORTUNISTIC INFECTION PROPHYLAXIS[16,17]

Pneumocystis carinii pneumonia (PCP) is currently the most common opportunistic infection, despite the fact that it is preventable with the use of prophylactic trimethoprim/sulfamethoxazole (Bactrim). One double-strength Bactrim a day is over 95% effective at preventing PCP. Women may tolerate Bactrim better than men. Many individuals with a history of an allergy to Bactrim can tolerate daily Bactrim prophylaxis. Alternatively, patients can be desensitized with an oral desensitization regimen. All individuals should begin PCP prophylaxis when their CD4 count is <200, or CD4 percent <14%, or when they present with thrush or chronic unexplained fevers. An alternative to Bactrim for patients who are persistently intolerant includes dapsone (100 mg P.O. daily) or aerosolized pentamidine, which is a third choice. Atovaquone is currently being evaluated for systemic prophylaxis. Bactrim fortunately also is effective as prophylaxis against *Toxoplasma gondii* encephalitis in persons with positive toxoplasma antibody titers and CD4 cells <100; it may also prevent some bacterial infections. During the past decade, aggressive prophylaxis and more effective treatment of opportunistic infections have contributed more than antiretroviral therapy to prolonging and improving the quality of life among patients with HIV and CD4 counts <200.

Mycobacterium avium complex (MAC) is the second most common cause of opportunistic infection. MAC occurs in the setting of profound immunosuppression: the mean CD4 count at the time of MAC bacteremia is 12. Prophylaxis with either Rifabutin at a dose of 300 mg/day or Clarithromycin

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at a dose of 500 mg B.I.D. appears to be approximately 50% effective in preventing MAC bacteremia. MAC bacteremia is associated with fever, progressive anemia, hepatic involvement manifested by an elevated alkaline phosphatase, and wasting. The ability to decrease the incidence of MAC is encouraging. Recommendations as to when to begin MAC prophylaxis have varied; many clinicians elect to begin MAC prophylaxis at a CD4 count of 50 as the incidence of MAC bacteremia increases substantially with lower CD4 counts.

Prophylaxis of severely immunocompromised patients with systemic azoles such as fluconazole has dramatically decreased the incidence of *Candida esophagitis* and cryptococcal meningitis. However, as patients live longer with profound immunosuppression and CD4 counts under 50, the incidence of *Candida mucositis* resistant to fluconazole is increasing. The benefits of fluconazole prophylaxis (a dose of 100 mg a day) increase substantially in patients with CD4 counts <50 because it is in these patients that the risk of *Candida esophagitis* and cryptococcal meningitis is high. Fluconazole may be used episodically to treat Candida mucositis at higher CD4 counts, but the cost and risk of developing resistant candidiasis outweigh the benefits of chronic prophylaxis in patients with higher CD4 counts.

Bacterial pneumonia is exceedingly common among persons with AIDS. It is the leading life-threatening infection among women with AIDS and the fourth leading life-threatening infection among men. The most common etiologic agents are encapsulated bacteria such as *Streptococcal pneumonia* and *Hemophilus influenza*. The response to prompt antibacterial therapy is excellent. It is critical that all individuals with HIV infection receive pneumococcal vaccine every five years. The earlier pneumococcal vaccine is given, the more effective the immune response, so vaccination should occur at the first visit.

HIV infection alters the natural history of tuberculosis so that patients who are HIV positive are more likely to contract tuberculosis. The presentation may be atypical, and the development of symptomatic disease more rapid. On the other hand, response to appropriate therapy is good. Tuberculosis appears to be entirely preventable in persons who are HIV positive if latent TB infection is detected. All individuals who are HIV positive should undergo skin testing with PPD and anergy panel testing. A positive PPD (defined as 5 mm of induration - not 10 mm, as in HIV negative persons) should immediately trigger institution of preventive therapy with Isoniazid (INH) and pyridoxine (B6) for one year.

Therapy must be monitored to ensure compliance. Likewise, any history of TB exposure in a patient who is anergic or with a history of a positive PPD at any time in the past should trigger preventive therapy. In patients who are anergic, a yearly chest x-ray is important for detection of disease.

The incidence of CMV retinitis and CMV gastrointestinal disease (esophagitis and colitis) is increasing among individuals with HIV as persons live longer with CD4 counts <50. Therapy of CMV end organ disease has relied upon intravenous gancyclovir and foscarnet. The recent licensing of oral gancyclovir for treatment of CMV retinitis in patients with AIDS gives clinicians an additional option for therapy. After persons with CMV retinitis were induced with IV gancyclovir for three weeks, oral gancyclovir was just as efficacious as IV gancyclovir for maintenance therapy.[18] Unfortunately, progression of retinitis occurred in approximately two months in patients on maintenance, therefor, patients must be monitored very closely. The finding that oral gancyclovir is safe and effective as maintenance therapy is encouraging, as it may delay the necessity of placing long term intravenous access in patients initially diagnosed with CMV retinitis.

The risk of CMV retinitis increases dramatically with CD4 counts < 50. In the future, we may be able to predict which patients are at greater risk for CMV disease using measures of CMV viral load. This would allow the development of markers that would enable development of better prophylactic regimens.

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SUMMARY

The second wave of the HIV epidemic, which increasingly affects injection drug users, women, and minorities, necessitates the development of primary care HIV services so that these individuals may benefit from new therapies. The ability to dramatically decrease vertical transmission of HIV from mother to child with antiretroviral therapy is encouraging. Better understanding of HIV pathogenesis, disease progression, antiviral therapy, and opportunistic infection prophylaxis are leading to more effective therapy and prevention. Clinical trials are ongoing to assess the efficacy of protease inhibitors in combination with nucleoside analog antiretroviral therapy to provide long term viral suppression and alter the natural history of HIV. Prophylaxis of pneumocystis, toxoplasma, MAC, TB, and invasive fungal infections is cost effective and leads to improved quality of life.

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Fibromyalgia

John R. Parziale, MD, and Joseph J. Chen, ScB

Fibromyalgia is a common disorder, causing chronic muscular pain and fatigue, affecting between 3,000,000 to 6,000,000 individuals in the U.S. The estimated prevalence of fibromyalgia ranges from 0.7% to 3.2% of the population. Of those affected, 80% are women between 20 to 50 years of age. Women are affected 8 to 20 times more often than men.[1]

First described by Balfour in 1824 and Valleu in 1841, fibromyalgia is characterized by tender points and trigger points in multiple areas, usually along large muscles or muscle-tendon insertions. Stockman (1904) reported muscular nodules that are "inflamed, tender, and if large, can be easily felt." Gowers coined the term "fibrositis" in the same year. No histologic features of the nodules could be found at that time, and many authors concluded that fibromyalgia was psychogenic in origin. The disorder, which had ill-defined characteristics, was known by many names, including fibrositis, myofascial pain, muscular rheumatism, and tension myalgia.

Fibromyalgia is a chronic diffuse musculoskeletal pain syndrome in which the overriding symptom in the majority of patients is widespread musculoskeletal pain. Patients may describe diffuse myalgias, polyarthralgias and pain in the neck, mid and lower back. Patients often describe the pain in graphic terms such as sharp, aching, burning, or cramping, with detailed descriptions of its quality, intensity and radiation. Pain may be more severe in one location than another or occur in "waves" of generalized musculoskeletal discomfort. An important characteristic of fibromyalgia as a distinct syndrome is the concept of its fluctuating course.

> *Although fibromyalgia is often a chronic condition, it can be successfully treated in many patients.*

Generally, patients with fibromyalgia, will have a cyclic pattern of pain with "good days" and "bad days." However, most patients have some degree of pain each day. It is important to recognize that there are modulating factors in fibromyalgia. The pain is usually aggravated by cold or damp weather, poor sleep, intercurrent illness, lack of exercise, trauma, and physical or psychological stress. However, there are factors that should ameliorate the symptoms of fibromyalgia. These include: warm/dry weather, restful sleep, heat application and modest exercise (Table 2).

In addition to musculoskeletal pain, patients with fibromyalgia have a variety of associated symptoms. These include headaches, paresthesias of the extremities, cold intolerance, subjective swelling of the hands or feet, abdominal pain or cramping and non-restorative sleep.

The American College of Rheumatology established diagnostic criteria for fibromyalgia in 1990 which predicted a sensitivity of 88% and a specificity of 81% in diagnosing fibromyalgia. These criteria include: (Table 1)

1. History of widespread muscular pain involving pain in both left and right sides of the body, pain above and below the waist, and pain in the neck, chest or low back.
2. Pain in 11 of 18 tender point sites (Figure 1) on digital palpitation (occiput, lower cervical trapezius, supraspinatus, second rib, lateral epicondyle, greater trochanter, media knee),[2]

Table 1
American College of Rheumatology
1990 Diagnostic Criteria for Fibromyalgia

1. Chronic muscular pain of at least three months duration.

2. Pain in 11 or more tender points within 18 characteristic locations:

- Occiput
- Lower Cervical
- Trapezius
- Supraspinatus
- Second rib
- Lateral epicondyle (elbow)
- Upper gluteal border
- Greater trochanter (lateral thigh)
- Medial knee

ABBREVIATIONS USED

ACR	American College of Rheumatology
ADP	Adenosine 5-biphosphate
AMP	Adenosine monophosphate
ATP	Adenosine triphosphate
CPK	Creatine phosphokinase
CSF	Cerebrospinal fluid
EEG	Electroencephalogram
EMG	Electromyogram
HIAA	Hydroxyindolylacetic acid
NSAID	Non-steroidal anti-inflammatory drug
PC	Phosphoryl creatine
REM	Rapid eye movement
SSRI	Selective serotonin re-uptake inhibitor

Table 2
Factors Affecting Fibromyalgia Symptoms

Aggravating Factors
- Cold or damp weather
- Poor sleep
- Intercurrent illness
- Lack of exercise
- Trauma
- Physical or psychological stress

Ameliorating Factors
- Warm or dry weather
- Restful sleep
- Application of heat to affected muscles
- Modest exercise

The diagnosis of fibromyalgia requires a careful history including the elements mentioned above. On physical examination, the patient should not have evidence of arthritis or a neurologic disturbance. However, trigger points can be identified in the substance of large muscles, over bony prominences and at the points of attachment of ligaments to bone.

Endocrinopathies, systemic rheumatic disorders, metabolic or hematologic conditions and neurologic syndromes may present with symptoms of fibromyalgia. It is important to rule out such disorders with a careful history and physical examination and judicious use of laboratory studies. (Table 3)[3]

The etiology of fibromyalgia is unknown. A variety of theories have been developed to explain its pathogenesis (Table 1). These include abnormalities of the usual sleep cycle, disorders of muscle metabolism, disturbances of neurotransmitters and the hypothalamic-pituitary axis and psychopathologic mechanisms. (Figure 2)

SLEEP DISORDERS

An important pathophysiologic characteristic of fibromyalgia is a disturbed sleep cycle. Normal sleep involves cycles of four non-dream stages known as Non-REM sleep alternating with dream stages called REM (Rapid Eye Movement) sleep. These five stages repeat in a cyclical manner every 45 to 60 minutes. The four stages of Non-REM sleep progress from light sleep in Stage I to deeper, more relaxing sleep in Stage IV. In Stage IV sleep, EEG activity predominantly represents delta-waves indicating deepest sleep. Delta waves are presumed to be necessary for restoring muscles histochemically.

Alpha waves are normally seen when people are resting or sleeping lightly. Moldofsky has described alpha-wave intrusion of delta sleep[4]; Alpha waves interrupt the normal delta waves and produce a deprivation of restorative Stage IV sleep. When reproducing the same Stage IV sleep deprivation in normal controls, some controls began feeling the onset of musculo-skeletal pain in the classic tender point distribution. Deprivation of sleep in healthy people, in particular those with a poor physical fitness level may elicit transient symptoms similar to fibromyalgia. Moldofsky reasoned that aerobic fitness is capable of modulating the contribution of altered sleep pattern to symptoms characteristic of the fibromyalgia syndrome. Sleep studies of individuals meeting the ACR criteria for fibromyalgia may demonstrate characteristic alpha wave intrusion into Stage IV sleep, though this is not uniformly seen. While alpha-delta sleep is not a marker of fibromyalgia, it may contribute to the illness of some patients with fibromyalgia. This phenomenon may explain why many fibromyalgia patients describe awakening every 45 to 60 minutes. This concept of disordered alpha-delta sleep as the causative agent has been recently challenged.

Table 3
Differential Diagnosis of Chronic Muscular Pain[10]

Fibromyalgia
Myofascial pain syndrome
Arthritis (rheumatoid or osteoarthritis)
Chronic fatigue syndrome
Rheumatic diseases (systemic lupus erythematosus, Sjogren's syndrome, ankylosing spondylitis)
Myopathies (polymyositis, dermatomyositis, myasthenia gravis, Eaton-Lambert syndrome)
Disc herniation
Polymyalgia rheumatica
Other (sleep apnea, reactive hypoglycemia, hypothyroidism, anemia, diabetes mellitus type II, and malignancy)

DISORDER OF MUSCLE METABOLISM

The theories of the pathogenesis of fibromyalgia include a contribution of microcirculatory ischemia, indicating a lack of oxygen and blood flow to muscles. Exercising muscle has reduced blood flow in patients with fibromyalgia, as compared with controls. Lund showed decreased oxygen tension over trapezius tender points consistent with a maldistribution of capillary blood flow. ATP, ADP, and PC levels are decreased in the trapezius of fibromyalgia patients, as compared to normal subjects. Eccentric non-physiologic contraction of sarcomeres may produce a functional shortening of muscle causing the characteristic decreased range of motion and muscle stiffness.

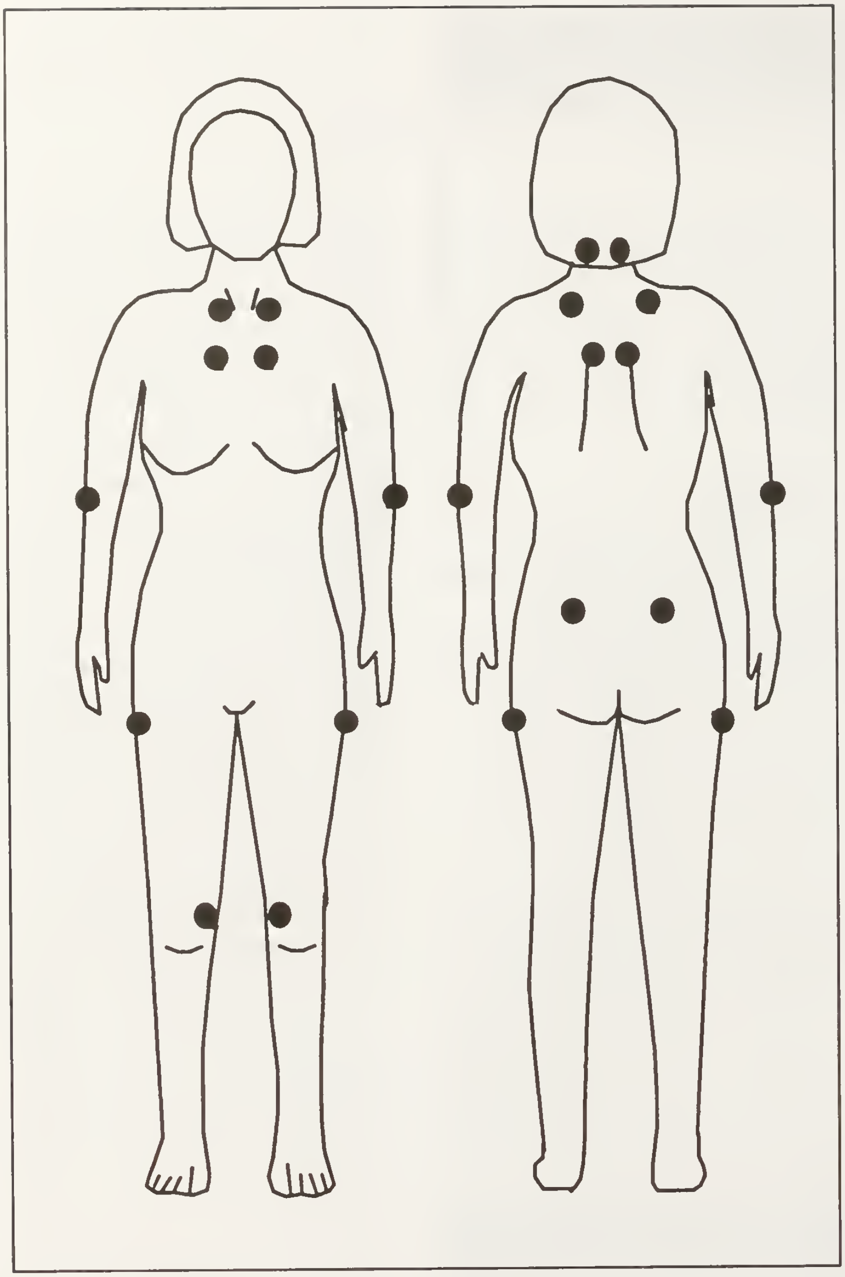

Figure 1: Tender Points Recommended for Diagnosis of Fibromyalgia

The aerobic capacity of fibromyalgia patients has been shown to be below average as compared with age and gender-matched subjects in the general population. Many patients with fibromyalgia are reluctant to undergo vigorous physical activity due to complaints of chronic muscle stiffness and pain. When deconditioned normal subjects undergo vigorous physical activity, most will experience post-exertional pain, 24 to 48 hours after the activity. Fibromyalgia patients seem to experience this same reaction, although on a more severe level.

HISTOLOGY

Bartels and Jacobsen described a "rubber band" morphology in needle muscle biopsies of individual muscle fibers, using this morphologic feature resulted in a specificity of 71% and a sensitivity of 63% in diagnosing fibromyalgia patients. Other studies show no evidence of abnormalities by light microscopy, histochemistry, or immunoenzye procedures; but upon electron microscopy, Drewes described discrete ultrastructural changes as "empty sleeves" of basement membrane and lipofuscin inclusions.

EMG

EMG studies in fibromyalgia patients are unremarkable; an abnormal study characterized by myopathic potentials or diffuse fasciculations is not consistent with this diagnosis.[5] Some fibromyalgia patients have difficulty relaxing their muscles. This inability to relax stressful muscles may play a role in muscle pain in those muscles prone to injury performing repetitive motions.

NEUROTRANSMITTER IMBALANCE

Campbell *et al* reported that the pain threshold of fibromyalgia patients at the diagnostic tender points was lower than in normals, but was not decreased in non-diagnostic sites on the body. Increased pain perception also may be related to increased CSF Substance P found in patients with fibromyalgia.[6] These finding suggest that fibromyalgia may be a disorder of pain modulation.

An alternative hypothesis involving serotonin metabolism proposes an association between low levels of tryptophan and fibromyalgia symptomatology. Russell noted decreased levels of tryptophan in patients with fibromyalgia. Tryptophan is a precursor to serotonin, which is involved in enhancing stage IV sleep and in the inhibitory descending pain pathways. Fibromyalgia patients have decreased CSF levels of 5-HIAA, a metabolic product of brain tryptophan metabolism.

PSYCHOPATHOLOGIC MECHANISMS

It has been postulated that many of the symptoms of fibromyalgia result from depression and somatization disorders. Indeed, patients with fibromyalgia are more likely to be clinically depressed compared to normal controls or age-matched controls with other illnesses. The majority of patients with fibromyalgia, however, are not clinically depressed, and depression in fibromyalgia is frequently a consequence of, rather than a pre-disposing factor to chronic pain.

LABORATORY TESTS

Routine laboratory studies in fibromyalgia are essentially normal. Tests to determine metabolic causes of chronic muscular pain include: com-

Table 4
Treatment of Fibromyalgia

1. Diagnosis and reassurance
2. Avoidance of aggravating factors (eg ,cold, narcotics, steroids,)
3. Workplace modifications
4. Pharmacological options (eg, sleep regulator, NSAIDs)
5. Physical modalities (eg, heat, massage, sprays, anesthetics, and injections)
6. Recreational aerobic exercise
7. Patient's active role in treatment

plete blood count, erythrocyte sedimentation rate, electrolytes. thyroid function tests, CPK and aldolase. If the patient has evidence of arthritis or symptoms of a systemic connective tissue disease, then a rheumatoid factor or antinuclear antibody test may be appropriate. These studies are used to determine the presence or absence of systemic inflammatory conditions. Fibromyalgia can be an initial presentation of hypothyroidism, and symptoms can be improved by replacing thyroid hormone. Sleep studies may show alpha intrusion into delta sleep on EEG recordings of Stage IV or non-REM sleep in some patients. The EMG is usually normal. Muscle histopathology shows minor abnormalities, including few or no inflammatory cells and Type II fiber atrophy. Theories involving decreased ATP and ADP phosphorylain, increased AMP and creatine levels, and local hypoxia have been suggested. ATP abnormalities, however, have been refuted. Routine biopsy of muscles or anatomic trigger points is not recommended.

MANAGEMENT STRATEGIES

A first step in managing the individual with fibromyalgia is making an accurate diagnosis. Many patients have seen multiple physicians, without a clear diagnosis or explanation of their constellation of symptoms. A careful explanation to the patient of the concept of fibromyalgia is important. Patients should be informed that the prognosis of fibromyalgia is generally good, but that pain may be chronic. Providing educational material to patients is frequently helpful.

In treating fibromyalgia, physicians have used a combined approach of: (Table 4)

- Diagnosis and reassurance,
- Avoidance of aggravating factors (eg, cold, narcotics, benzodiazepines, etc.),
- Pharmacological options (sleep regulator, NSAIDs, etc.),
- Exercise.

The most important strategy in treating fibromyalgia is to interrupt the cycle of pain and fatigue. In general, the longer the duration of pain, the more difficult it is to interrupt the cycle. An important initial step is to control the disturbed sleep cycle. Treatment of Stage IV sleep deprivation with low dose cyclobenzaprine or amitriptyline has been shown to increase Stage IV sleep and decrease pain and tender points.[7] Non-steroidal anti-inflammatory drugs can be helpful to alleviate local symptoms. Pain control using narcotics or corticosteroids should be discourage based on currently available information. Chabal has shown that oral mexilitine can be an effective analgesic in some patients with chronic pain refractory to other medical treatments. Investigational field trials using mexilitine, which reduces muscle membrane depolarization by blocking ion transport channels, have shown promise. In a small group of patients with severe muscle tenderness due to fibromyalgia, 50% demonstrated improved function and reduced pain levels on mexilitine (unpublished). The use of selective serotonin re-uptake inhibitors (SSRI's) such as fluoxetine also have been studied. Preliminary results have shown that his agent has modest promise. Medications such as sertraline and paroxetine also are currently being investigated.

Physical modalities such as heat, massage, sprays, topical anesthetics or trigger point injection, stretching and flexibility exercises, light aerobic conditioning, and biofeedback can be helpful. Injection of a limited number of painful tender trigger points with a lidocaine/corticosteroid solution has been used to provide temporary reduction in pain. A regular stretching program for relatively pain-free muscles also is important for continued control of myalgias. Supramaximal contraction of these muscles can be associated with muscle injury.

Recreational aerobic exercise such as cycling or fast-walking has been shown to help reduce symptoms and improve sleep and muscle fitness. In one study of the therapeutic potential of aerobic conditioning in patients with fibromyalgia, an aerobic conditioning group improved their pain threshold scores, as compared to controls. No improvement in sleep disturbances were reported. Based on these results, a hypothesis that exercise confers symptom relief through anxiolytic effects and the promotion of restorative sleep through enhanced serotonin levels has been promoted.

Workplace modification can often be helpful in reducing symptoms. Individuals with fibromyalgia have difficulty tolerating jobs that require overhead assembly, using a computer for key entry or typing, or playing a keyboard.[8] Working night shifts may further aggravate the sleep disturbance in fibromyalgia patients. Excessive visual and auditory stimulation has been observed to aggravate fibromyalgia. Many patients also describe exacerbation of their symptoms by working in a cold, drafty environment.

It is important that the patient be instructed in the implementation of the treatment program and the goals of therapy. It also is essential that the patient becomes directly involved in his/her treatment program. With a clearly explained diagnosis, patients can re-direct their fears and frustration into an appropriate rehabilitation regime. Cog-

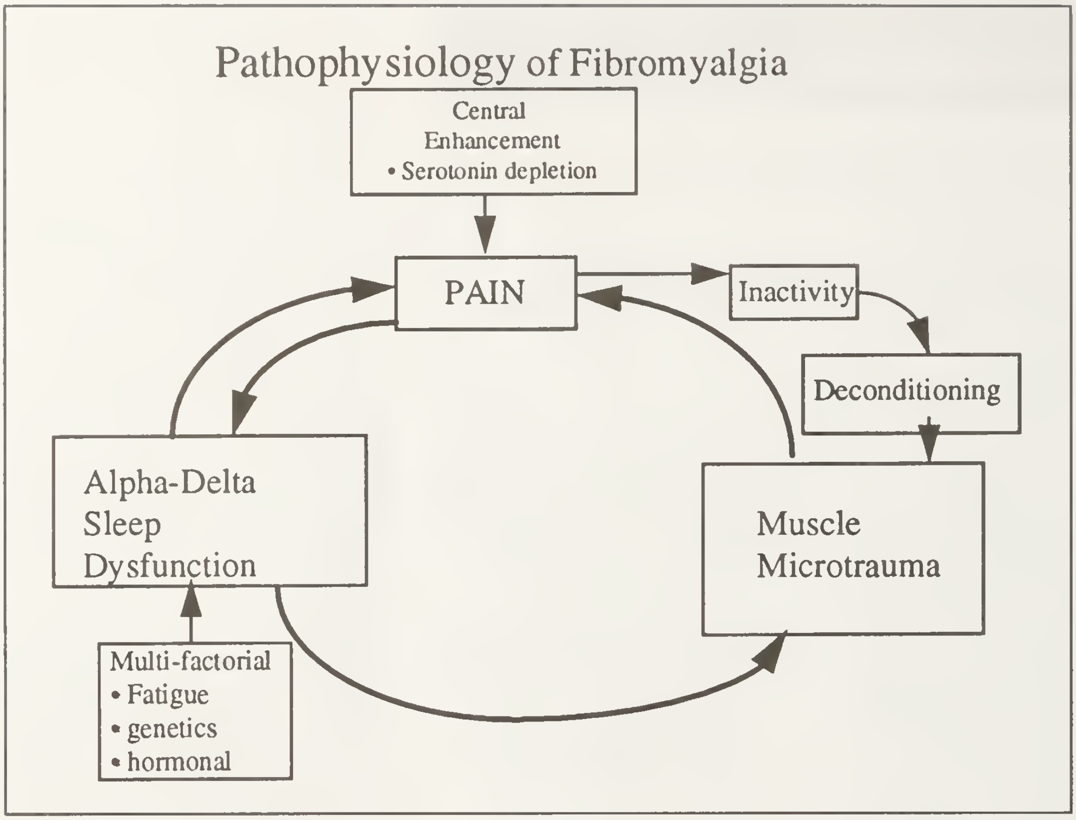

Figure 2: Pathophysiology of Fibromyalgia

nitive behavioral therapy, stress reduction, relaxation response training, and teaching the importance of self-help also have shown some effect.

The physician, affected employee, and employer need to work together to avoid situations that may aggravate this condition. This requires an understanding of the nature of fibromyalgia and the type of activities that should be avoided. Local fibromyalgia support groups, in-house exercise and relaxation programs or job task rotation during the workday may all prove to be helpful.[8]

PROGNOSIS

The newly-diagnosed patient with fibromyalgia must be reassured that he/she does not have a life-threatening or disfiguring illness. Most individuals are relieved to know that their constellation of symptoms is identified and can be treated.

Even with adequately controlled sleep and medications, some individuals will remain chronically symptomatic. Recent studies offer hope by showing that many patients with fibromyalgia will have fewer symptoms after sleep has been corrected. In a study of 44 patients with fibromyalgia enrolled in a regimen of regular physical exercise, 47% no longer fulfilled the ACR criteria for fibromyalgia after two years, and 24% were in remission. Reassurance, counseling, medications, and exercise are essential to the long-term management of fibromyalgia.

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Public Health Briefings

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Judith Feldman, MD, MPH, and John P. Fulton, PhD

Physical Activity and Health

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The health benefits of physical activity are myriad. As recently summarized by Fentem in the *British Medical Journal* (Table 1), physical activity enhances functioning of the skeletal muscles, tendons, connective tissue, and joints, promotes cardiac rehabilitation and helps control minor mental illness, helps prevent coronary heart disease, stroke, osteoporosis, non-insulin dependent diabetes mellitus, and obesity, and preserves physical and mental functioning in the elderly.

The promotion of leisure-time physical activity is strongly advocated in the medical literature and in national public health consensus recommendations for the year 2000. Nonetheless, at least three major issues central to the promotion of physical activity are currently under scrutiny in the medical literature.

HOW MUCH IS ENOUGH?

Early last year the American College of Sports Medicine and the Centers for Disease Control and Prevention (ACSP/CDCP) published a landmark recommendation for physical activity, asserting that 30 minutes of moderate physical activity per day would produce significant health benefits for most people. Shortly thereafter, results were published from the Harvard Alumni Study which seemed to contradict the ACSP/CDCP recommendation. The longevity of Harvard alumni was observed to be directly related to the amount of sustained, vigorous physical activity they had performed; a similar effect was not observed for moderate physical activity. Who was correct? Had the benefits of moderate physical activity been exaggerated by the ACSM/CDCP, or had the Harvard Alumni Study somehow missed those benefits? The issue was raised in letters to the editor and generally made good press.

Actually, the two publications are not very contradictory. Both acknowledge the health benefits of "moderate-intensity physical activity" or "non-vigorous exercise," and both make the point that engaging in more vigorous physical activity nets greater health benefits for participants than less vigorous physical activity.

The main difference between the two is one of emphasis. The ACSP/CDCP recommendation emphasizes the health benefits which accrue at the lower end of the activity-intensity spectrum, while acknowledging the added benefits of more vigorous physical activity. The report from the Harvard alumni study emphasizes the longevity benefits which accrue at the upper end of the activity intensity spectrum, while acknowledging the health benefits of less vigorous physical activity.

The rationale for the ACSP/CDCP emphasis is rooted in the knowledge that many people have remained sedentary, thus eschewing all the health benefits of moderate intensity physical activity, because they cannot envision themselves maintaining a program of vigorous physical exercise over time. This is especially unfortunate, because the greatest increase in health benefit occurs at the lower end of the activity spectrum. The ACSP/CDCP recommendation is intended to maximize the effect of health promotion to increase physical activity by focusing on persons who have the most to gain by a small behavior change.

The two reports differ largely in their interpretation of non-contradictory evidence for the effect of physical activity on longevity. The ACSP/CDCP recommendation cites evidence from six studies that the relative risk of cardiovascular mortality is monotonically related to level of fitness or physical activity, and infers from the evidence as presented that much of the physical activity measured in the studies may have been intermittent and of moderate intensity. The Harvard Alumni analysis builds on previous studies by teasing out the separate longevity effects of performing vigorous and nonvigorous activity, revealing that energy expended on vigorous physical activity is related to age-standardized mortality from all causes, while energy expended on moderate physical activity is not. Evidence from the Harvard Alumni study appears to refine rather than contradict previous evidence, but probably warrants replication before concluding that previous studies would have shown the same effects, had they distinguished vigorous from nonvigorous physical activity.

DOES THE PHYSICAL ACTIVITY OF EMPLOYMENT COUNT?

The assessment and promotion of physical activity in the general public frequently focuses on leisure time physical activity. When this approach is taken, certain groups, notably low income minorities, appear to be in great need of physical activity, and would naturally become the preferred targets of programs to promote leisure time physical activity.

Critics of this approach assert that when assessing the need for leisure time physical activity, the physical activity of employment must be used in the equation as well. For example, persons

Table 1
Benefits of Exercise in Health and Disease[1]

Skeletal muscle functions
- Increased stamina
- Increased capacity for work and exercise

Tendon and connective tissue functions
- Strength
- Supportive function
- Joint stability

Joint functions
- Lubrication
- Range of movement

Skeletal functions
- Maintenance of bone mass
- Adjustment of structure to load

Metabolic functions
- Control of body weight
- Improved carbohydrate tolerance
- Inhibition of blood clotting processes

Psychological functions
- Reduced mild anxiety and depression
- Improved self esteem
- Improved psychomotor development
- Improved memory in the elderly

Control of cardiovascular disease
- Reduced risk of coronary heart disease and stroke
- Improved cardiac rehabilitation
- Reduced risk of sudden death in coronary heart disease

Control of other diseases and physical dysfunction
- Reduced risk of osteoporosis
- Improved control of blood glucose in non-insulin dependent diabetes mellitus
- Reduced risk of breast and colon cancer? [Suggested by recent research]
- Control of physical disability attributable to age or chronic disease

who perform hard physical labor at work five days per week would need little or no leisure time physical activity to accrue the health benefits attributed to moderate intensity physical activity, and possibly those attributed to vigorous intensity physical activity, as well. From this perspective, employed low income minorities, who probably engage in more physical activity as blue collar workers than employed middle and upper income groups do as white collar workers, may require less, possibly far less, leisure time physical activity than the latter groups to accrue the health benefits attributed to physical activity.

In a response to one such criticism, Pate *et al.*, authors of the recent ACSP/CDCP recommendation, acknowledge that "physical activity performed in the occupational setting is expected to be as beneficial as that performed during leisure time." They go on to assert, however, that "the trend toward decreasing occupational physical activity is profound and seems unlikely to reverse," and predict that "future increases in physical activity will occur primarily during leisure time."[3]

WILL MUSCULOSKELETAL INJURY LIMIT INCREASES IN PHYSICAL ACTIVITY?

Promoting increased physical activity produces injurious as well as beneficial effects. People who increase physical activity also increase the risk of musculoskeletal injury. Those who are injured may avoid physical activity in the future. Even the threat of injury may serve as a barrier to physical activity among some individuals, especially those with pre-existing health problems. In their landmark recommendation, Pate *et al.* list injury as "a common reason for stopping regular activity."[3] In a further acknowledgement of this problem, however, Pate asserts that "one benefit of promoting moderate-intensity physical activity, as emphasized in the recommendation, is its relatively low risk of musculoskeletal injury," citing two studies on injury related to leisure time physical activity. To minimize the negative effect of such injury, Pugh, Waller, and Marshall suggest1) including basic injury prevention messages when promoting physical activity (to help prevent injury), and 2) assuring access to sports medicine services (to facilitate recovery and return to a full physical activity program), "particularly for those not usually considered athletes." They concluded, "Although the risk of physical activity-related injury exists, we believe the benefits of any increase in the physical activity of our sedentary society outweigh this risk."

DO RISKS OUTWEIGH BENEFITS FOR PERSONS AT RISK OF CVD?

A recent editorial in the *New England Journal of Medicine* posed a critical question for all those at risk of cardiovascular disease: "Is exercise beneficial - or hazardous - to your heart?" The editorial accompanied the reports of two studies on the subject. Both found an increased risk of myocardial infarction (MI) in patients who engaged in sudden bouts of strenuous physical activity. Both, however, also found that patients who engaged in regular physical activity had a lower increased risk of MI related to strenuous physical activity than patients who were less active. In short, regular, moderate-intensity physical activity may lower the risk of MI from strenuous physical activity, supporting the importance of gradual increases in the intensity of physical activity, especially among persons at risk of cardiovascular disease.

PHYSICIAN: EXERCISE THYSELF!

Pate *et al.* speak directly to physicians in the "Call to Action" that accompanied the recent ACSP/CDCP recommendation: "Physicians and other health professionals should routinely counsel patients to adopt and maintain regular physical activity. Physicians can be effective proponents of physical activity because patients respect physicians' advice and change their exercise behaviors as a result. The large number of primary care physicians and the frequency with which Americans visit them suggest that even modestly effective physician counseling would have a substantial public health impact."[3] They go further, however, to encourage physicians to become personally immersed in the issue: "The personal physical activity practices of health professionals should not be overlooked. Health professionals should be physically active not only to benefit their own health but to make more credible their endorsement of an active lifestyle." A very good idea, indeed!

MOVE IT YOUR WAY ...

A group of health agencies in Rhode Island known as the Prevention Coalition (of which the Rhode Island Department of Health is a founding member) recently decided to focus on the promotion of physical activity as one of the most practical and significant contributions to the public's health in Rhode Island. The Coalition adopted two objectives from *Healthy Rhode Islanders 2000*:

- 60% of people aged 6 and older will engage regularly in light to moderate physical activity for at least 30 minutes per day.
- 85% of people aged 6 and older will engage in some leisure-time physical activity.

The Prevention Coalition hopes to involve organizations of all types from throughout the State in their endeavor to get Rhode Islanders moving. Perhaps it is most fitting to close with their call to action, announced in January:

Move it your way. Move it any way. Just move it!

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Health by Numbers

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Jay S. Buechner, PhD and William J. Waters, Jr., PhD

Workplace Smoking Policies of Rhode Island Employers, 1995

Robert R. Vanderslice, PhD, Deborah D. Bercovitch, Estel S. Alves, and Susan J. Hester

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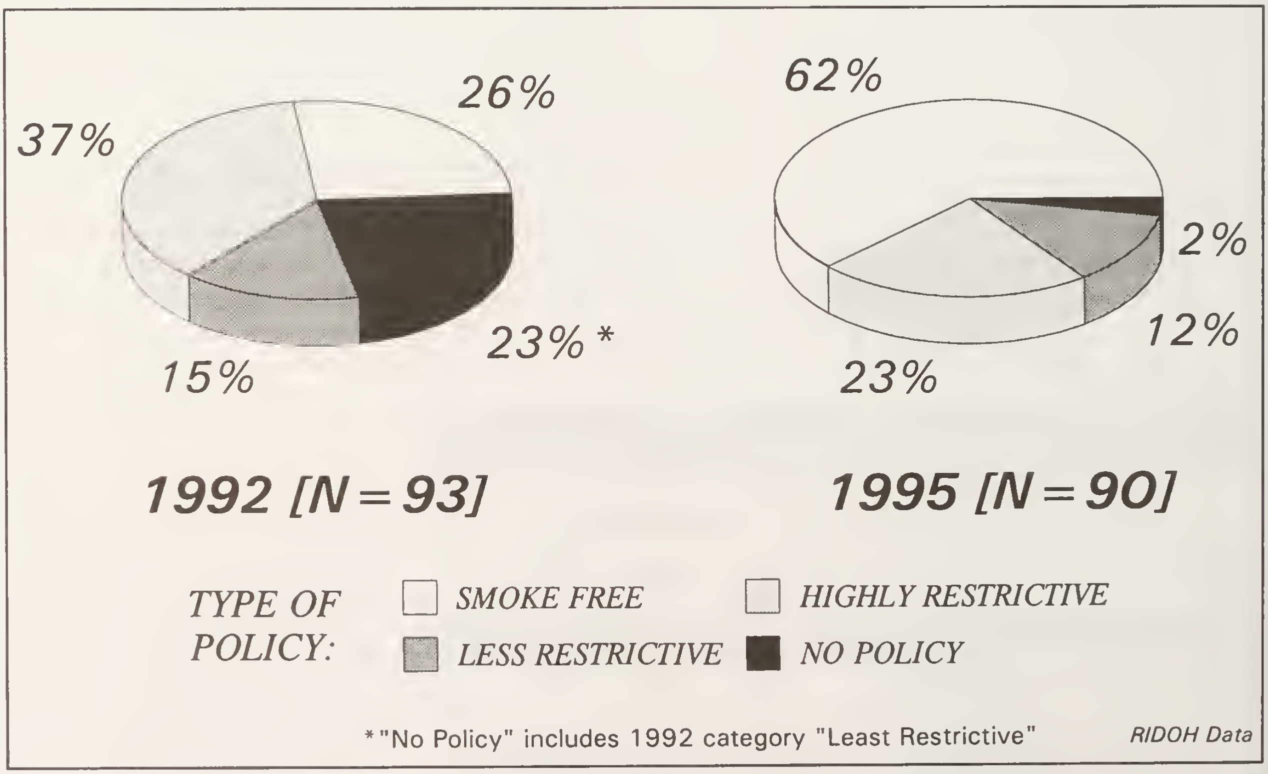
Environmental tobacco smoke remains one of Rhode Island's leading environmental health risks. Environmental tobacco smoke, also called ETS or second-hand smoke, has been classified by the United States Environmental Protection Agency as a known human carcinogen. Because of these hazards, limiting occupational exposure to ETS is a national health objective for the year 2000.[1] To determine the current status of workplace smoking policies in Rhode Island companies, a telephone survey was conducted recently by the Rhode Island Department of Health (RIDOH), Office of Environmental Health Risk Assessment.

METHODS

The RIDOH surveyed a representative sample of ninety businesses, chosen systematically from two sources. Thirty-four were selected from the 607 businesses listed in *Major Employers In Rhode Island*, (Rhode Island Department of Economic Development, Research Division, February 1995), and fifty-six were selected from the 2,776 businesses listed in the *Rhode Island Directory of Manufacturers*, (Rhode Island Department of Economic Development, Economic Research Division, March 1993.) These two sources were chosen to include information from both manufacturing and non-manufacturing firms. Because there was no single source available for small non-manufacturing firms, they were not included in this survey. Each company contacted was questioned using a standard telephone survey protocol, similar to the protocol used by RIDOH in its 1992 survey of the workplace smoking policies of Rhode Island employers.[2] The person most knowledgeable regarding company policy was interviewed at each of the businesses. In addition to questions regarding the policy itself, the respondent was asked about the availability to employees of smoking cessa-



*"No Policy" includes 1992 category "Least Restrictive"

RIDOH Data

Figure 1. Smoking policies of Rhode Island employers, 1992 and 1995.

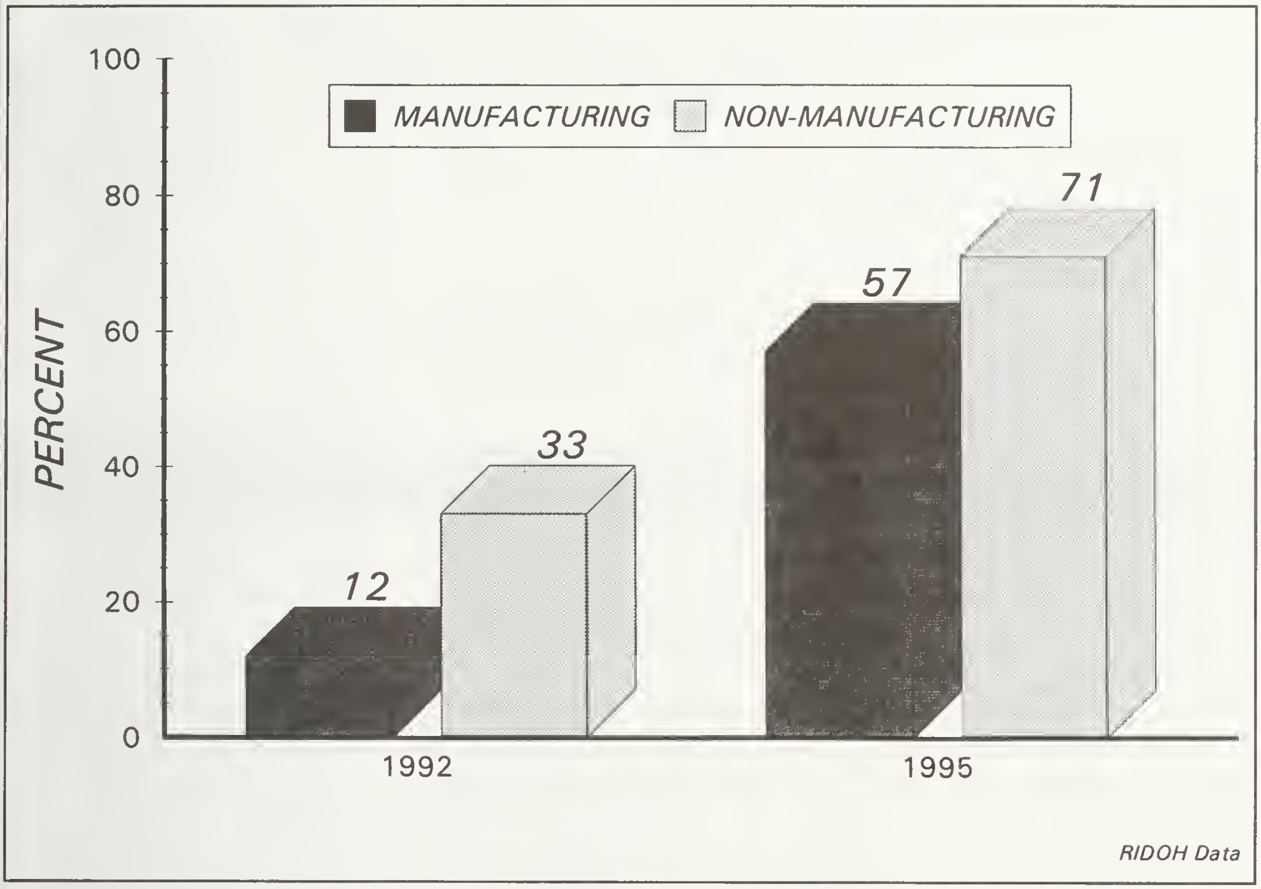


Figure 2. Percentage of Rhode Island employers with smoke-free workplaces, by type of industry, 1992 and 1995.

tion programs. Companies which did not have a workplace smoking policy were given information on the Rhode Island Workplace Smoking Pollution Control Act of 1986, which requires that all Rhode Island employers adopt, implement, and maintain a workplace smoking policy.

Workplace smoking policies were categorized in the following manner: "smoke free" (no smoking allowed anywhere on indoor company property), "highly restrictive" (smoking permitted only in a section of the workplace such as a smoking lounge, cafeteria, or private office), "less restrictive" (smoking permitted in any of the following areas: corridors, bathrooms, conference rooms, stairwells, and/or certain offices), and "no policy" (smoking issues are not addressed either officially or unofficially by management). It is possible that a company might have a workplace smoking policy which provided no restrictions on smoking; however, no such policy was reported.

RESULTS

Eighty-eight (98%) of the 90 companies contacted had workplace smoking policies. Sixty-two percent of the companies surveyed reported being "smoke free", 23% were "highly restrictive", and 12% were "less restrictive." (Figure 1) Non-manufacturing firms generally were more likely to have restrictive policies than manufacturers. Non-manufacturing firms were found to be 71% "smoke free", while 57% of the manufacturing firms reported being "smoke free." (Figure 2) Non-manufacturing firms were found to be 26% "highly restrictive" and 3% "less restrictive". In contrast, manufacturing firms reported being 21% "highly restrictive" and 18% "less restrictive". Four percent of the manufacturing firms had no policy, whereas all non-manufacturing firms had policies in place.

The restrictiveness of the policy may correlate with business size. All of the non-manufacturing firms surveyed had 100 or more employees and comprised the most restrictive business category, with 71% of establishments "smoke free". Of manufacturing firms with 50-99 employees, 65% were "smoke free"; of those with 100 or more employees, 60% were "smoke free"; and of those with 1-49 employees, 44% were "smoke free". In general, larger firms were more likely to have an official "smoke free" environment than smaller firms.

The 1995 RIDOH survey sampling strategy was similar to that of the RIDOH survey conducted in 1992. Ninety-three companies were included in the 1992 survey, while ninety were surveyed in 1995. An analysis of trend data shows that the percentage of manufacturing firms which have a smoke free policy has increased from 12% in 1992 to 57% in 1995. Non-manufacturing firms also showed a substantial jump in the percentage of companies with smoke free policies, from 33% in 1992 to 71% in 1995. Only 3% of companies reported no workplace smoking policy currently, a drop from 10% in the 1992 RIDOH survey.

In addition to creating a smoke free or restricted smoking environment, many employers are also making concerted efforts to help their employees quit smoking. Fifty-one percent of all of the surveyed companies now offer employees access to a smoking cessation program. These programs vary and include participation in in-house classes (20%), classes offered through the company's health insurance (9%), programs offered by non-profit organizations (4%), hospital-based programs (3%), and miscellaneous other programs. In addition, some companies (8%) offer reimbursement to employees for the cost of other approved cessation programs. One of the surveyed companies offered a bonus for those employees who remained smoke free for a predetermined amount of time.

A breakdown of the companies by size indicates that 6% of small manufacturers offer cessation programs, while 35% of medium manufacturers and 80% of large manufacturers offer this benefit to employees. By type of industry, 43% of manufacturers and 65% of non-manufacturers have taken formal steps to help their employees quit smoking.

DISCUSSION

This survey shows that workplace smoking policies in Rhode Island have become significantly more restrictive since the RIDOH survey done in 1992. The previous survey reported that 26% of Rhode Island businesses had "smoke free" policies (compared to 62% in 1995), 65% had "restrictive" policies (35% in 1995), and 10% had "no policy" (2% in 1995). Rhode Island workers are increasingly protected by their employers from the health hazard of exposure to environmental tobacco smoke. In addition, it is possible that increasing the number of businesses that restrict smoking in the workplace will cause a decrease in tobacco use outside the workplace. A study published in "Tobacco Control" found that "...workplace smoking restrictions provide a means by which many smokers will reduce their daily cigarette consumption...."[3] As the behavior of smokers becomes modified in the workplace, smoking habits both inside and outside the workplace are expected to change, creating fewer smokers and a healthier environment for all Rhode Islanders.

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Vital Statistics

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Roberta A. Chevoya

Rhode Island Monthly Vital Statistics Report
Provisional Occurrence Data from the Division of Vital Records

Vital Events

	Reporting Period		
	Nov. 1995	12 months Ending with Nov. 1995	
	Number	Number	Rates
Live Births	994	13,738	13.8*
Deaths	769	9,708	9.7*
Infant	(7)	(99)	7.2#
Neonatal	(5)	(81)	5.9#
Marriages	491	7,270	7.3*
Divorces	278	3,641	3.7*
Induced Terminations	415	5,739	417.7#
Spontaneous Fetal Deaths	98	1,114	81.1#
Under 20 weeks gestation	(94)	(1,048)	76.3#
20 + weeks gestation	(4)	(66)	4.8#

* Rates per 1,000 estimated population
# Rates per 1,000 live births

Underlying Cause of Death

	Reporting Period			
	May 1995	12 Months Ending with May 1995		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	307	3,277	328.9	4,661.5
Malignant Neoplasms	180	2,426	243.5	6,866.0
Cerebrovascular Diseases	58	613	61.5	652.5
Injuries (Accident/Suicide/Homicide)	20	322	32.3	6,553.0
COPD	34	409	41.1	285.0

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.
(b) Rates per 100,000 current estimated population of 996,325.
(c) Years of Potential Life Lost (YPLL).

Note: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

THE RHODE ISLAND MEDICAL JOURNAL
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Ninety Years Ago

May, 1906

The lead article represents Dr. Frank L. Day's Presidential Address presented at the annual meeting of the Providence Medical Association. Dr. Day chose to provide the membership with a detailed history of the Association with particular emphasis upon its beginnings, which he traced to a little room on North Court Street where Dr. H.W. Rivers had his medical office. There on a Monday evening on the last day of January, 1848, the physicians of Providence met to take steps toward the formation of a medical association "for the mutual benefit of its members." At that time, Providence was a city of 40,000, with about 50 doctors. The Association adopted four stipulated goals: First, the separation of the regular and irregular practitioners; second, the creation of an Association for "the purpose of mutual recognition and fellowship;" third, the promotion of the character, interests and honor of the fraternity, by maintaining the unity and harmony of the regular profession; and fourth, the cultivation and advancement of the science by presenting pathologic cases and specimens for mutual study.

Charles L. Scudder, MD, a surgeon from Boston, presents a paper on a newly described entity, stenosis of the pylorus in babies. The author provides a synopsis of prior cases in the literature before summarizing his own experience. He first details the typical history elicited from the mother of such an afflicted child; and then he outlines the usual physical findings, particularly distinguishing this entity from other causes of periodic vomiting in the neonatal interval. Finally, he discusses therapy, insisting that a medical approach (ie, non-surgical) will almost invariably fail. Surgical intervention, in his judgment, is the only path to pursue, despite a surgical mortality rate of about 50%. The approach that he advocates is the posterior gastroenterostomy, with rapidity of surgery, ample incision and the exercise of very great care to avoid loss of blood, with no soiling of the peritoneum and the handling of bowel as little as possible.

Fifty Years Ago

May, 1946

Francesco Ronchese, MD discusses the value of the Wood light as a diagnostic aid in the recognition of ringworm of the scalp and other dermatoses. The Wood lamp (named for the American physicist, R.W. Wood) employs a source of ultraviolet light passing through a nickel oxide filter which removes visible light waves. The ultraviolet rays which pass through the filter will then selectively cause certain substances and organisms to fluoresce. This procedure is of distinct value in identifying scalp ringworm but it is also of value in diagnosing *tinea versicolor* (as distinguished from leukomelanodermas) and the macular syphilides. The following fungi will fluoresce with Wood's light excitation: virtually all microsporons, and species of *Trichphyton* and *Malassezia*.

A symposium on acute respiratory diseases, moderated by Alex Burgess, MD is summarized. Harold Calder, MD discusses acute respiratory diseases from the standpoint of the pediatrician, emphasizing the clinical features of such entities as croup and follicular tonsillitis. Francis B. Sargent, MD discusses upper respiratory infection as seen by the laryngologist. Guidelines for the use of sulfa drugs and penicillin are provided. Finally, Morgan Cutts, MD considers acute respiratory infections from the internist's viewpoint, stressing the rational use of antibiotics and the proven value of the new influenza vaccine.

The Rhode Island Medical Society officers for 1946-47 are announced: Arthur H. Ruggles, MD as president-elect; Michael H. Scanlon, MD as vice-president; Morgan Cutts, MD as secretary; Charles J. Ashworth, MD as treasurer; Charles B. Seppi, MD as assistant secretary; and G. Raymond Fox, MD as assistant treasurer.

Twenty Five Years Ago

May, 1971

The lead article, representing an extensive and rigorous epidemiological study of a cluster of leukemia cases in North Kingstown, Rhode Island region, is authored by Lorrena Preble, MAT and Louis A. Leone, MD. The authors state: A total of 14 cases of leukemia (10 acute, 4 chronic) have occurred in North Kingstown in an 11 year, 4 month period extending from January, 1959 through April, 1970. Nine cases of acute leukemia and three cases of chronic leukemia have been recorded since 1996; the paucity of cases in earlier years is probably related to the improved methods of case finding instituted in 1966. The occurrence of 8 cases of acute leukemia from 1965-69 represents a highly significant statistical departure from the expected incidence adjusted for age based on a Poisson distribution, revealing that 8 cases of leukemia in ages 0-44 for the interval of 1965-69 would be expected to occur only twice out of 100. Hints were presented to suggest that interpersonal contacts of an indirect nature may have contributed to the epidemiological pattern observed in both the naval and civilian populations of the region.

Arnold Porter, MD, president of the Rhode Island Medical Society Physicians Service (Blue Shield) presents his yearly report, particularly as it pertains to cost control. He notes in passing that there is an increasing interest in proposals for the establishment of Health Maintenance Organizations (HMO's) as well as Professional Services Review Organizations (PSRO's).

Arthur Hanley, executive director of Blue Cross-Blue Shield discusses medical education, hospital construction, prospective reimbursement and state regulation of hospital costs in his annual report.

Officers of the Rhode Island Medial Society for 1971-72 are presented: William J. MacDonald, MD, president; Richard J. Kraemer, MD, vice-president; Robert V. Lewis, MD, president-elect; Stephen J. Hoye, MD, secretary; John P. Grady, MD, treasurer; Edmund T. Hackman, MD, AMA delegate; Seebert J. Goldowsky, MD, Editor-in-Chief of the Journal and alternate AMA delegate.

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Submission Requirements

Manuscripts should be typewritten, double-spaced with liberal margins. Authors also are asked to provide the manuscript and computer-generated graphics on a floppy diskette, formatted in either Microsoft Word or Word Perfect. If possible, Macintosh disks should be saved in DOS format, using Apple File Exchange.

Illustrations and charts must be submitted in black ink on white paper. Laser-printed graphs are acceptable, provided they are printed at 300 DPI resolution.

Photographs must be in black and white, submitted on 5" x 7" glossy paper.

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COMMENTARIES

Advances in the Treatment of Brain Tumors

No field of medicine has changed more over the past ten years as a result of technical advances than the specialty of neurological surgery. Sectional imaging with both the CT scan and the MRI scan has made precise diagnosis and localization painless, accurate and safe. The computer revolution, coupled with MRI scanners and other imaging modalities, now gives the surgeon instantaneous access to such previously unimaginable information processes as intraoperative tracking with a three-dimensional image of the patient's brain, clear visualization of the pathology and real-time position localization.

As Dr. Greenblatt's historical overview points out, the development of surgical techniques for treatment of brain tumors, linked directly to the introduction of essential technologies in anesthesia, antisepsis and cerebral localization, became a defining element in the early evolution of neurological surgery as a specialty. As Dr. Saris notes, current treatment for malignant gliomas involves a multidisciplinary approach in which surgery is supplemented by radiation (including both whole brain and radiosurgical approaches) and chemotherapy. Dr. Chougule reviews the somewhat different treatment options for patients with brain metastases, including an emerging role for gamma knife radiosurgery, while Drs. Friehs, Jackson and Duncan describe modern approaches to treatment of CNS tumor chronic pain, pituitary adenomas, and brain tumors in pediatric patients.

It is perhaps appropriate that the final article in this issue is written by Dr. Georg Noren, who during the late 1970's worked directly with Dr. Lars Leksell in Stockholm, Sweden, to develop the application of gamma knife radiosurgery to the treatment of acoustic tumors. Exemplifying the rapid coming together of several new technologies, the Leksell Cobalt 60 Gamma Knife, in which radiation is directed stereotactically to any location within the brain with uncanny precision and intensity, was only a dream a few years ago. This device, capable of treating previously unapproachable tumors or other pathology without the need for open craniotomy, has resulted from a melding of the principles of sectional imaging, computer dose planning and stereotactic surgery with the development of special collimators to focus radiation into fine beams.

As contributors to this issue, one of our primary goals has been to give readers of *Medicine and Health/Rhode Island* who are neither neurologists nor neurosurgeons some appreciation of the accelerating technology that has so rapidly changed this specialty in recent years and promises to change it even more in years to come. The other has been to provide balanced accounts of our specialty's professional interest in brain tumors with respect to both current approaches and the historical context from which they developed. We hope those readers will find that both of these objectives have been realized.

Mel H. Epstein, MD

The Art of the Fugue

Each profession painfully assembles its private vocabulary partly to define itself, partly to expedite communication within its ranks, and partly to establish territorial boundaries with competing guilds. Circumstances inevitably arise when a new word needs to be identified to describe a heretofore unknown event, technic or instrument. Sometimes a totally new word [neologism] is created; but more commonly, the needed term is selected from the common pool of available words and then endowed with special, often arcane, in-house meanings.

The formal terminology of one profession will inevitably overlap the chosen words of another - through accident, through respectful borrowing or sometimes by just plain usurpation. With the passage of time, of course, the same word will yield dramatically different meanings in the hands of separate groups.

Professions with similar tasks tend to share specialized terminology while the jargon of professions with disparate purposes customarily bear little in common. But even in professions as dissimilar as music and medicine one will inevitably find some sharing of technical terms.

For example, both musical sequences and red blood cells can display chromatic variations; and scales may characterize piano practice as well as patients with ichthyosis. Medicine defines a ligature as a suture tied around some tissue structure such as a blood vessel. In baroque music, however, it signifies a notation which incorporates two or more notes into a single symbol instructing the musician to play the notes in such close sequence that a slurring effect is produced. The Italian word for ligature, *legato*, is now the more commonly employed term for this musical effect. A fistula, in medicine, represents a pathologic passageway between two spaces. In music, though, it is the Renaissance name for the organ-flute. The Latin for key, *clavis*, in the domain of music, evolves into both clef [the sign on the musical staff indicating pitch] and the instrument, clavichord. In the world of anatomy it becomes the clavicle. Similarly, words such as copula, dactyl, organ and introit have distinguishable meanings depending upon the context in which they are uttered. Chords and tonics have legitimate - but widely separated - existences in each of the two professions. Upbeat can describe a happy spirit - or it can identify the first arm motion undertaken by a conductor. Percussion and tympany fit comfortably in the left rear of the symphony orchestra - but they are also at home in the restricted vocabulary of physical diagnosis. The concluding passage in a musical composition is called a coda, a word which has its origins in the anatomical *cauda* [Latin, meaning tail.]

The technical verbiage jointly employed by general medicine and music probably represent instances of chance overlap since there are more things to name in this world than available names. But one branch of medicine in particular, neurology, seems to share more words with music than its sister clinical disciplines; and this is almost predictable since both neurology and music concern themselves with movement, esthetic or pathologic.

Musical syncopation is defined as a series of planned, momentary displacements in the anticipated meter, inserting brief and deliberate pauses in the progress of the melody. The word is derived from the Greek meaning a cutting off [sometimes even signifying castration as in the word, capon.] Buried within syncopation is the medical term, syncope, meaning a momentary swooning or lapse of consciousness, literally a cutting off of cerebral circulation.

Ictus [Latin, meaning stroke or blow] represents a stress or accent in music, particularly in monophonic [Gregorian] chants. In medicine, however, it signifies an acute attack or intracranial stroke.

The choreography of classical ballet represents the epitome of graceful, deliberately coordinated movement. The chorea of Huntington's disease is anything but disciplined or gracious. It is hardly, in a word, choreographed.

To the neurologist, a fugue is an interval of utter forgetfulness, a dreamlike state often with elements of wandering, all of which may be aftermaths to motor seizures. The word conveys a sense of fleeing, of fugitive movement. Some patients have been known to wander for extended intervals, totally amnestic, with but scattered islands of retained memory. During these dissociative intervals purposeful but automatic acts may be undertaken by the patient. The disorder goes by many names including *epileptische Wanderlust*, ambulatory automatism and poriomania [Greek, *poriea* meaning a journey]. Hughlings Jackson described these episodes as epileptic somnambulism, the dreamy state or procursive epilepsy. Bing describes it as follows:

> Without the least motive, the patient suddenly leaves home or the work he is doing. He travels at random from city to city, and to the casual observer his behavior is quite normal. Upon subsidence of the episode the patient may feel as though he had awakened from a dream, the content of which he remembers dimly or not at all. [1]

The word fugue [Latin, *fuga*, meaning flight] also appears in the diagnosis, amaurosis fugax [a temporary blindness often associated with cerebral ischemia]. Here too there is a sense of a fleeting phenomenon. A musical fugue, on the other hand, describes a contrapuntal device consisting of a small number of "voices" each carrying a defined melody but sung serially rather than simultaneously. Again a fugitive transiency defines this novel musical technic.

An anthem [Greek, meaning a response and cognate to *anthera*, meaning a blossoming, a bursting forth, as in the word chrysanthemum] is customarily a stirring musical rendition often with liberal use of brasses. "The pealing anthem swells the note of praise" when it serves to inaugurate monumental public events. Medicine, not to be outdone in awesome terminology, has modified the word to depict the strident blossoming of skin rashes [such as in measles] - now calling them the exanthems.

In truth, however, there are remarkably few vocational words shared by medicine and music; perhaps an isolated word, here and there, but nothing more than can easily be accounted for by mere random overlap. And this should be so since the very purposes of the two professions, at a deeper level, diverge so substantially: Music strives for harmony; medicine, on the other hand, pursues its business in the reverse direction, seeking out dysfunction and physiologic dissonance; and should it perchance encounter bodily harmony, it hastily changes direction to pursue disorder elsewhere.

Stanley M. Aronson, MD

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* * *

Physicians Should Support Needle Exchange in Rhode Island

As the HIV epidemic continues to expand in the United States, it is clear that it is being driven by injection drug use. The Centers for Disease Control and Prevention (CDC) reported that, in 1981, 12% of new AIDS cases were attributed to injection drug use; by 1994, 36% of new AIDS cases were associated with injection drug use. Meanwhile, the number of AIDS cases within the category of "men who have sex with men" has declined steadily. In Rhode Island as of November 1995, at least half of the 2,585 reported HIV infections were related to injection drug use.

The primary mode of transmission among drug users is through the sharing of injection equipment. The CDC recommends that a new syringe and needle be used for each injection. If injection drug users were able to adhere to this standard, HIV transmission via this route would cease. However, the primary barrier to the spread of HIV through re-using and sharing needles is the availability of clean injection equipment.

There are two types of laws which limit availability of clean injection equipment: paraphernalia laws, which make it a criminal offense to possess injection equipment, and prescription laws, which require a prescription for the purchase and sale of new needles and syringes. Both of these laws, designed to combat drug abuse, have had the unintended effect of increasing needle and syringe sharing, and the subsequent spread of HIV. In some states, including neighboring Connecticut, these laws have been rescinded in an attempt to prevent HIV transmission.

One HIV prevention response has been to provide sterile needles and syringes to injection drug users through Needle Exchange Programs. These programs give out sterile injection equipment in exchange for used and contaminated syringes: in order to get a syringe, you must already have one. In addition, these programs provide an array of HIV prevention, medical and social services, and referral to drug treatment. For those people who cannot or will not stop injecting drugs, needle exchange programs are the most effective way to prevent HIV transmission.

Such programs have been enacted throughout Europe and the United States. Recent reports by the National Research Council, the Institute of Medicine and the CDC document the efficacy of such programs in preventing transmission and decreasing the risk of new HIV infections. An often cited concern about needle exchange programs is that they might increase drug use. These reports found no evidence of an increase in drug use due to these programs and found, in addition, that there is strong public support for Needle Exchange Programs which tends to increase over time. There are several additional benefits that can result from Needle Exchange Programs. By agreeing to use clean needles, injection drug users are taking an important first step towards improving their health, which may lead towards other steps, including drug treatment. The best HIV prevention for injection drug users would be to stop injecting drugs entirely. But until they have stopped injecting and have benefitted from drug treatment, which works for most injection drug users, we have a stake in preventing AIDS transmission. There is a big difference between a healthy ex-drug addict, and an ex-drug addict with AIDS whose spouse is HIV infected and whose children have AIDS.

In Rhode Island, needle exchange began in April 1995 as a pilot program approved by the state legislature and under the aegis of the RI Department of Health. It has steadily increased in enrollment and distribution of needles with over 250 clients enrolled and over 6,000 needles distributed. Unfortunately, at this magnitude, it is having but limited impact on the estimated 10,000 active injection drug users in our state. This program needs to be actively supported by the medical community. Clearly, the establishment of an expanded needle exchange program is a critical element to HIV prevention in Rhode Island. Physicians should be in the forefront, advocating this sound public health policy.

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The Role of Brain Tumors in the Establishment of Modern Neurosurgery

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Modern neurosurgery owes its existence to brain tumors. For the first 75 years of the specialty's life, from approximately 1880 to the decade of the 1950s, tumors were neurosurgery's paradigmatic problem and hence its defining theme. The early pioneers also struggled with congenital lesions, inflammatory diseases, pain, and trauma, but they did not establish neurosurgery as a distinct specialty until they could show that they had achieved truly remarkable outcome statistics with brain tumors.

Most historians of neurosurgery agree about the essential elements that defined the first modern neurosurgical operations, but there is a little controversy about when those elements first came together. A brief historical examination of the issue shows that ideas about brain tumors were at the center of those events.

The essential technologies for the founding of modern brain surgery were: anesthesia, antisepsis, and cerebral localization.[1] Anesthesia with ether and chloroform dates to the 1840s, and Lister's initial work with antisepsis was done in the 1860s. Modern localization started in 1861, with Broca's clinical and pathological description of the aphasic syndrome that bears his name. Hughlings Jackson began to define the physiological significance of the epileptic pattern that we now call the "Jacksonian march" in the late 1860s. Fritsch and Hitzig found the electrically excitable motor cortex in dogs in 1870, and Ferrier extended their experimental findings to primates in 1874.[2,3] In 1876, Ferrier published his monumental *Functions of the Brain*, which provided a compendium of animal localization data including proposed homologies between primates and humans.[4]

The surgeon who consciously combined these three essential technologies to do the first modern neurosurgical operations was William Macewen (1848-1924) of Glasgow, Scotland. In March 1879, he correctly localized and successfully removed a subacute right frontal subdural hematoma in a 9 year old boy who had a right frontal scalp contusion and left sided Jacksonian seizures.[5] In July 1879, Macewen localized and removed a left frontal *en plaque* meningioma in a 14 year old girl.[5] Although he had earlier removed a "swelling" of her left orbit, and there was a very small left frontal exostosis, he did not undertake the craniotomy until the patient manifested appropriately localizing right Jacksonian seizures. In 1883, Macewen also correctly diagnosed and successfully removed three more intracerebral lesions: a traumatic hematoma, a "syphilitic tumor" (gumma) in the paramedian rolandic cortex, and a small spontaneous intracerebral hematoma.[6]

Abbreviation Used

ICP	Intracranial pressure

When Macewen summarized these cases in 1888, he laid claim to priority in the initial utilization of cerebral localization to perform modern craniotomies:

> With the relation of these . . . cases, all of which occurred prior to the end of 1883, the initial history of the movement ceases to be solely personal as regards myself. In December, 1884, Dr.Bennett and Mr.Godlee, assisted by Dr.Ferrier, had the first case operated on in London in which a tumor was removed by Mr.Godlee from the brain.[6]

The Bennett and Godlee case, cited by Macewen, has traditionally been regarded as the beginning of modern neurosurgery.[7-10] In the mind of the medical public at the time, that was definitely how the event was perceived. In 1879, Macewen was a young (age 31) and unknown surgeon in a provincial Scottish city. His craniotomies were often conducted at odd hours and certainly with no fanfare. London, on the other hand, was the political and cultural capital of an empire on which the sun never set. Alexander Hughes Bennett (1848-1901) was also a young Scotsman, but he was practicing medicine in London and had an appointment at the Hospital for Epilepsy and Paralysis, Regent's Park.

In 1884, Bennett saw a 25 year old farmer who complained of progressive left hemiparesis, predominantly in the arm, with violent headaches and protracted vomiting. The man had Jacksonian seizures, generally beginning in the left arm, but sometimes in the left face and tongue. On examination, he had "double optic neuritis" (bilateral papilledema) and motor findings consistent with his complaint. The patient was admitted for diagnosis and medical treatment on November 3, 1884.

By the 1880s, Jackson and Ferrier were both active senior physicians at the Hospital. The published record shows that Ferrier saw the patient "before, during, and after" the surgery, but there is no evidence that Jackson was formally consulted. However, the Hospital was a small place, and there were probably informal discussions among the staff.[8] In any case, Bennett certainly understood Jackson's and Ferrier's principles of neurological diagnosis. He concluded that the patient had a small cortical tumor "in the neighborhood of the upper third of the fissure of Rolando."[7] Bennett asked Rickman J. Godlee (1849-1925) to operate. Godlee was Lister's nephew and assistant. Although he held no appointment at the Hospital for Epilepsy and Paralysis, where the surgery was performed, he was Surgeon to the nearby University College Hospital, London.

The patient was trephined on November 25, 1884, with several observers on hand, including Ferrier.

> . . . even after the bone was removed, the dura mater [was] slit up, and the cortex of the brain exposed, no tumor was visible. The ascending frontal convolution, however, seemed to be somewhat distended. An incision about an inch long was made into the grey matter . . . and a quarter of an inch below the surface a morbid growth was found. This was carefully removed, and proved to be a hard glioma about the size of a walnut.[7]

The patient awoke satisfactorily from the chloroform anesthesia. In the early postoperative period he had some left sided seizures and a major hemiparesis. The wound edges began to separate on the fourth postoperative day, and a cerebral hernia (fungation of brain through the wound) was seen on the fifth day. It was debrided rather vigorously, but he began to show signs of systemic infection on the twenty second day. He died on December 23, 1884, 29 days after the procedure.

Even before the final outcome was known, the Bennett and Godlee case evoked intense interest in the medical press, and some notice of it spread to the larger public newspapers. *The Lancet* was particularly attentive, giving its first brief notice in its issue of November 29. On December 20, 1884, *The Lancet* proclaimed:

> This operation, performed, we believe, for the first time in the history of medicine, has naturally attracted much notice amongst the profession . . .[7,11]

The case was discussed in the London *Times* and other newspapers because of its implications for the contemporary debate on vivisection.[12] Ferrier was known to the general public in this regard, because he had been unsuccessfully prosecuted under the British antivivisection laws in 1881. The medical community was quick to point out that it was his experiments that had provided the scientific basis for the possibility of curing brain tumors in suffering human beings.[13]

The newspapers in Glasgow, alerted by the debate in the *Times*, quickly rose to the defense of Macewen's priority in this important achievement of modern medical science.[14] The arguments in favor of Bennett and Godlee's priority boiled down to two factors: (1) In some of Macewen's cases there were external signs of the disease process, although Macewen really did not rely on them, and (2) the lesion in Bennett and Godlee's case was somehow a more real tumor problem, because it was small and arose from intrinsic brain tissue; as such, it could not have any external markings.[9]

The patient's death diminished the doctors' enthusiasm only slightly. They did not seem to acknowledge the direct connection between the tumor and its treatment, on the one hand, and the brain fungus and infection on the other, though Godlee understood it.[8] In part, this apparent dissembling can be attributed to their very limited comprehension of intracranial pressure phenomena, which have come to be understood only in the twentieth century. But they also had a legitimate reason to celebrate. The tumor had been found and removed, so the potential to do the same thing again - hopefully with success - was clearly at hand. In fact, this was a valid assumption, because Macewen had already done it, and so had Francesco Durante (1844-1934) in Rome in May, 1884.[15]

The essential technologies for the founding of modern brain surgery were: anesthesia, antisepsis and cerebral localization.

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In the wake of the Bennett and Godlee case, a wave of enthusiasm for doing "brain cases" spread through Europe and North America. A variety of pathologies was attacked, but brain tumors were the paradigm, partly because they had to be diagnosed on purely clinical and physiological grounds, since there were seldom any reliable external signs, as there might be in brain abscesses or trauma. The usual practice pattern was similar to that of Bennett and Godlee. A neurologist diagnosed and localized the tumor and then called in a surgeon to operate. Even if the tumor were found, the surgeons used general surgical techniques on cerebral tissue, and the results were predictable.

By the 1890s, the initial wave of excitement was followed by a wave of nihilistic depression. Mortality rates of 50% and more were reported regularly, even from such prominent centers as von Bergmann's clinic in Berlin.[16] Of equal interest to us and to the participants at the time was the quality of survivals after craniotomies for suspected or proven tumor. In an important series of mortality and morbidity surveys by an American, Phillip C. Knapp, this was expressed simply as percentage of patients not benefitted by their operations, and it was high.[17,18] Many bright young surgeons who might have made worthwhile contributions to neurosurgery were too daunted by its difficulties to pursue work in the field.[19]

It is perhaps not surprising to note that each of the important personalities in the emerging field of neurological surgery was quite young (early to mid 30s) when he made his initial contribution, for the same is true of the next major contributor, the American Harvey Cushing (1869-1939). To say that he was blithely undaunted by the difficulties would be grossly inaccurate, because his writings and his biography show that he had some doubts and many hesitations.[20,21] For any person of sound mind, it could hardly have been otherwise, and Cushing had a keen and ambitious mind.

In 1901, Cushing joined the surgery faculty at The Johns Hopkins University, where he had trained from 1896 to 1900. His chief was William S. Halsted (1852-1922), who pioneered surgical subspecialization by encouraging it among his faculty. Nonetheless, Cushing had to plead his case quite forcefully before Halsted agreed to let him specialize in surgical diseases of the nervous system.[21,19] Although Cushing made a formal announcement of his fulltime commitment to neurosurgery in 1904, he later admitted that in 1905,

> . . . tumor cases were few and far between in the Johns Hopkins clinic, and though at that time there had been no successful extirpations, we had begun to feel somewhat encouraged regarding the beneficial effects of purposeful decompressive measures.[22]

Those "decompressive measures" were a critical part of the new methodology that Cushing worked out and applied to "brain cases" from 1901 to 1910 and beyond. Over this period, he was able to achieve rapidly improving results because he combined meticulous aseptic technique with gentle Halstedian methods of tissue-handling. Conceptually, he then used these techniques to carry out operations that were designed to manage raised intracranial pressure (ICP) initially and only thereafter to find and remove intracranial masses. He understood the challenge of raised ICP because he had done extensive experimental work on the phenomenon from 1900 to 1903.[19] Cushing's success was thus derived from his new understanding of the pathophysiological difficulties, which in turn led him to develop better surgical strategies for operating on suspected brain tumors.

Cushing's tumor practice began to thrive in 1908; by 1910 he had operated on 180 tumors.[22] In the 100 cases immediately preceding his 1910 report, his mortality rate was 11%, and it was only 6% in the most recent 50 patients. When he moved to the Peter Bent Brigham Hospital and the Harvard Medical School in 1912, his entire practice essentially followed him, but it was interrupted by his military service in World War I. Nonetheless, he continued to analyze his experience, so he was able to give a paper on brain tumor statistics for a meeting of the American College of Surgeons in October, 1919.

Unfortunately, the complete text of this important presentation was never published, so the only available record of it is a medical reporter's summary.[23] Cushing focused on the difficulties of creating meaningful statistics, which raises the issue of how to define a brain tumor: Is a tuberculous gumma a tumor or is it something else? It is not clear that he actually gave his own statistics in 1919, but he did give them in a similar report in 1915, so we can reasonably surmise that they were not too much different four years and a world war later.[24] In 1915, when other large centers in the United States and Europe were still reporting mortality rates in the range of 20% to 50%, Cushing's operative mortality rate for his Boston series was 7.3%!

Regardless of the exact details, Cushing's 1919 report must have been an impressive performance, because:

> at its conclusion, [the chairman of the session] Dr. [William J.] Mayo rose and solemnly announced: "Gentlemen, we have this day witnessed the birth of a new specialty - neurological surgery."[25]

As a result of this exciting event, the world's first neurosurgical organization - the Society of Neurological Surgeons - was founded in 1920. Thus, the medical profession's recognition of neurosurgery as a distinct entity can be dated to 1919-1920.[1,19] First and foremost, though by no means exclusively, neurosurgery was the specialty that dealt with brain tumors. Tumors remained the central focus of neurosurgery's efforts to improve its own techniques and outcomes until after World War II and into the 1950s.

However, from very early in the twentieth century, many surgeons and others who dealt with these lesions realized that surgery was not the complete or final answer to the problem. External beam radiotherapy was applied to brain tumors in the first decade of the this century, and many series were reported in the 1920s, including some rather forbidding mortality rates.[26] Pancoast reported implantation of radium seeds as early as 1914, and series of such patients were reported in the 1920s.[27] In 1921, the American pathologist, James Ewing, concluded on histological grounds that gliomas should be more sensitive to radiotherapy than meningiomas or metastases.[28,26] In the early 1930s, the American neurosurgeon Ernest Sachs and the German Wilhelm Tönnis both reported that they were giving radiotherapy postoperatively for glioblastomas, although they were less than enthusiastic about the results.[26,29]

As the accompanying papers in this journal will show, we are still struggling with many of the fundamental problems that perplexed our predecessors when the twentieth century - and neurosurgery - were still young.

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Multidisciplinary Approach to Malignant Gliomas

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OVERVIEW

Approximately 15,000 primary malignant brain tumors are diagnosed each year in the United States. The majority of these tumors originate from the glial, or supporting, cells of the brain. In adults, malignant tumors originating from neurons (neuroblastoma, ganglioglioma) are extremely uncommon.

The three types of glial cells are astrocytes (which may help to regulate the blood-brain barrier and assist in the brain's immune system), oligodendrocytes (which supply myelin to the axons), and ependymal cells (which line the walls of the ventricles). Therefore, the three types of tumors are astrocytomas, oligodendrogliomas and ependymomas. The astrocytic tumors are subdivided into astrocytoma, anaplastic astrocytoma (AA), and glioblastoma multiforme (GBM) depending on the degree of malignancy.

The vast majority of primary malignant brain tumors originate from astrocytes. As described in detail below, the two common forms of these malignant astrocytomas are the anaplastic astrocytoma and the glioblastoma. These are the tumors that will be addressed in this article.

EPIDEMIOLOGY

Primary malignancies of the brain are relatively uncommon, constituting only about 2% of all cancers diagnosed per year in the United States. In 1985, 8 cases per 100,000 males and 5 cases per 100,000 females were diagnosed. However, due to an increase in the incidence of these tumors over the past several years, central nervous system malignancies have been designated as a priority disease by the United States Congress. The National Cancer Institute has funded three consortia of medical centers in order to rapidly investigate new therapeutic agents as they become available. Rhode Island Hospital - along with Johns Hopkins, Massachusetts General Hospital, Northwestern, Henry Ford, and Columbia-Presbyterian Hospital - is involved in one of these cooperative groups.

ABBREVIATIONS USED

AA	Anaplastic astrocytoma
BCG	Bacillus Calmette Guerin
BCNU	Bis-nitroso-urea
CT	Computed tomography
GBM	Glioblastoma multiforme
MRI	Magnetic resonance imaging
RTOG	Radiation Therapy Oncology Group
XTR	X-ray therapy

RISK FACTORS

Malignancies of the brain are second to the leukemias as the most common cancers in children. The occurrence in children less than 5 years of age is 3 cases per 100,000. The incidence tapers to 2 cases per 100,000 in the 10-14 year age group, and then gradually increases throughout adult life to a maximum of 20 cases per 100,000 between the ages of 75-79. Males are 1.5 times more likely to develop a nervous system malignancy than females. Caucasians are 1.5 times more likely than African-Americans to develop a nervous system malignancy. The incidence is highest among white males, with an incidence of 8 new cases per 100,000. In comparison, the lowest incidence is in black females, with an incidence of 4 cases per 100,000.

Other than in certain well-defined syndromes, the risk of developing a brain malignancy in first degree relatives of patients with gliomas is not increased. A number of familial aggregations of gliomas have been described; however, no chromosomal abnormality or pattern of inheritance has been demonstrated. Gliomas have been associated with certain inherited conditions such as neurofibromatosis (optic glioma, astrocytoma) and tuberous sclerosis (subependymal giant cell astrocytoma, gliomatosis cerebri).

PRESENTATION

The presenting signs and symptoms of nervous system malignancies depend on the tumor type and location. In general, tumors of the cerebral hemispheres usually present with local irritation of grey matter (seizures), destruction or swelling of the brain (weakness, sensory changes, abnormalities of vision, difficulty with speech), or elevated intracranial pressure (headache, nausea & vomiting, personality change). The lower grade of malignancy (astrocytoma) tends to present with seizures, while the higher grade tumors (glioblastoma) more commonly present with headache although seizures, focal neurological deficits, and personality change are not uncommon. It should be noted that the new onset of focal seizures in an adult is due to a brain tumor until proven otherwise.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of a brain tumor is determined by its location, the age of the patient, and its appearance on MR imaging. In adults, infections (brain abscesses) and metastatic tumors may be confused with primary brain malignancies. This highlights the need for a careful clinical assessment and a tissue diagnosis when evaluating these lesions.

DIAGNOSTIC WORKUP

In addition to a detailed history, the neurologic and general medical exam is important in evaluating a patient with a nervous system neoplasm. The neurologic exam often helps in the anatomic localization of the lesion, and the medical exam may give a clue as to a source for a possible abscess or primary tumor that might have generated the brain metastasis. No blood test aids in the diagnosis of primary brain tumors.

A non-contrast and contrast head CT scan is the most readily available test to evaluate a patient for the presence of a nervous system neoplasm. In the patient who has a seizure or developed a neurologic deficit, one looks for focal abnormalities in the brain which may enhance or cause edema. When performed with gadolinium, MRI is the most accurate test to image lesions in the brain. The anatomic detail is superb and multiplane imaging is available (coronal and sagittal as well as axial). Lesions in the posterior fossa are much better characterized by MRI because of the absence of bone artifact. Nuclear medicine scans usually have no role in the workup of brain neoplasms except when metastatic disease is being considered. In this case, a bone scan may identify lesions elsewhere in the body that might be more accessible for a surgical or needle biopsy.

Diagnostic Procedures. When the diagnosis of brain tumor is suspected, lumbar puncture is contraindicated until a head CT or MRI has been performed. If a large intracranial mass or non-communicating hydrocephalus is present, a lumbar puncture can cause tentorial herniation and death. However, this procedure is useful in the evaluation of medulloblastomas or ependymomas that are not associated with hydrocephalus or mass effect in the posterior fossa. The presence of malignant cells indicates dissemination of the tumor in the spinal fluid.

In many cases, stereotactic biopsy is the simplest method of obtaining a tissue diagnosis, and usually can be performed under local anesthesia. It is ideal for deep cerebral hemisphere lesions and can be done with a complication rate of less than 2% and a diagnostic accuracy of 96%. The procedure involves attaching a metal stereotactic device to the patient's head. A contrast head CT or MRI is performed, and with the use of a computer and the stereotactic device, three-dimensional coordinates for the lesion are calculated. A small needle is passed into the lesion through a small hole drilled in the skull. Biopsies are sent to pathology for histologic diagnosis. This procedure is contraindicated if a vascular lesion such as an aneurysm or arteriovenous malformation is suspected. In such cases, an arteriogram should be performed first.

Staging. Staging is generally used for cancers that spread regionally via the lymphatics, or distantly via the bloodstream. This is not applicable to gliomas because the brain does not have a lymphatic system and hematogenous dissemination is rare.

Treatment of Primary Brain Malignancies

The treatment options for malignant gliomas are surgery, radiation, and chemotherapy. Patients with malignant gliomas have a variety of unique problems that are best managed in a multidisciplinary manner. The team of caring physicians includes the neurosurgeon, neuro-oncologist, radiation oncologist, medical oncologist, and neuro-oncology nurse. In treating these difficult malignancies, as much attention needs to be directed to the quality as to the length of life. These patients have a need for careful monitoring of anticonvulsant medication, minimizing use of steroids, frequent brain imaging to determine if the tumor is under control, and participation in a support group whenever possible.

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Surgery. Surgery is indicated for purposes of diagnosis, reduction of elevated intracranial pressure, and reduction of mass effect. Even the most careful preoperative assessment of patients with enhancing intracerebral masses cannot distinguish between primary neoplasms, abscesses, and metastatic tumors. Given the minimal risk of surgery (combined major morbidity and mortality < 15%), we feel strongly that there is no substitute for a tissue diagnosis. This is invaluable in treatment planning and patient education. In addition, debulking a recurrent tumor to decrease the "tumor load" prior to chemotherapy or XRT has been of demonstrated benefit in retrospective, but controlled clinical studies.

The location of a neoplasm dictates the operative approach. Supratentorial lesions are generally approached by a craniotomy directly over the lesion if possible. Posterior fossa masses are generally approached by a midline incision over the occipital bone and dissection through or around the cerebellum. The approach to these tumors can often be guided with advanced technology such as the Elekta wand. This is a probe which when put into the brain will cause a crosshair to appear on an MRI of the patient one is operating on. This allows a safe approach to the tumor and avoidance of critical brain structures.

Craniotomy with total resection is the goal of aggressive surgery; however, if the tumor extends into important areas of the brain, such as Broca's area or the motor cortex, one may intentionally leave tumor behind rather than injure the patient. Gliomas cannot be completely resected. Even though a "gross total" removal (where all tumor seen at surgery is removed and no residual tumor enhances on post-operative CT or MRI scans) can be performed, the tumor is always infiltrative and microscopic tumor cells are left behind. In the 1930's, hemispherectomies were occasionally performed for these tumors. However, in 1-3 years the tumor would recur on the other side of the brain because glioma cells have a remarkable capacity to migrate along white matter pathways to locations far distant from what is thought to be the tumor margin.

Radiation. The role of radiation in the management of malignant brain tumors depends on the tumor histology. In the past, patients with gliomas traditionally were given 4500 cGy of whole brain radiation therapy followed by a 1500 cGy boost to the tumor. Currently, many centers are irradiating only the tumor plus a margin of 3 centimeters. Parts of the brain that have no tumor on CT or MRI are avoided.

Although generally regarded as the optimal treatment after surgery for malignant gliomas, the efficacy of radiation therapy is limited. In a large randomized trial conducted by the Brain Tumor Study Group, the median survival of treated patients was extended only by about six months. There is some evidence that a radiosurgical boost with the gamma knife may increase the effectiveness of adjunctive radiation by extending median survival another 3-6 months. This is being investigated in a national, randomized study by the Radiation Therapy Oncology Group (RTOG). The result of this trial will hopefully be available within a few years.

The incidence of acute complications from radiation therapy has been reduced by dose fractionation schemes and concomitant use of steroids. Daily fractions of about 180 cGy (rads), with a total dose to the brain of 50 - 60 Gy, are generally well tolerated. Occasionally patients develop increased swelling in the region of the tumor which can cause a neurologic deficit, mild somnolence and headache. In addition, this can result in transient worsening of their neurologic condition which spontaneously recovers in a few weeks. Radiation-induced brain necrosis is an uncommon and delayed reaction and occurs 1-2 years following radiation. It is diagnosed when a patient with a glioma deteriorates many months after radiation. The CT scan or MRI shows a new enhancing mass which can resemble either radiation-induced necrosis or recurrent tumor. Reoperation is undertaken, and necrotic brain is encountered.

Chemotherapy. Chemotherapy has been used as therapy following surgery and radiation therapy for malignant gliomas, not in lieu of radiation therapy. It is a sad comment that Bis-nitrosourea (BCNU) was first used in the early 1950's for the treatment of malignant gliomas, and still remains the most effective chemotherapeutic agent for this disease. In prospective, randomized, controlled studies, it prolongs survival by a few months as compared to surgery and radiation alone, and addition of other drugs to BCNU has not increased survival.

Given the limited efficacy of chemotherapy, the National Cancer Institute has embarked on a screening program which rapidly investigates new agents. There is current enthusiasm for two classes of agents topoisomerase inhibitors and anti-angiogenesis drugs. The former inhibits a nuclear enzyme essential for tumor cell replication. The latter inhibits the formation of blood vessels which is essential for development and growth of the tumor. This approach has been extremely effective *in vitro* and in animal models and studies are now underway to use these agents administered either systemically or directly into the tumor via a polymer implant.

Immunotherapy. Despite the attractiveness of this form of therapy, innumerable studies have shown absent or minimal efficacy. These include active immunotherapy with BCG, with parvum and glioma cell extract immunization; and passive treatment with interferon, peripheral blood lymphocytes, and activated lymphocytes. Although formidable amounts of research have been devoted to this approach, at present it has no role in the treatment of malignant brain tumors.

Gene therapy. Use of molecular techniques to treat malignant gliomas is currently in the earliest stages of development. The genetic mechanisms by which normal astrocytes transform and become malignant are just now being analyzed and understood. It is to be hoped that improvements in patient survival will be realized as a result of our more complete understanding and deliberate disruption of these processes.

The only trials currently underway involve injection of strands of genetic material in a viral envelope directly into the tumor. These genes are often able to become incorporated into the genome of the tumor cell, rendering them susceptible to drugs given intravenously. Early data suggest that this treatment is safe and may cause tumor regression in some patients. The laboratories in the Neuroscience Program at Brown are committed to this new line of therapy which hopefully will combat the infiltrative portion of the tumor when local control has been established.

PROGNOSIS

The prognosis for patients with malignant brain tumors depends on the tumor type and grade. It should be emphasized that malignant gliomas are amongst the worst cancers that occur in patients. The mortality from these diseases is virtually 100%, although some large series report occasional cures in less than 0.5% of patients. Given enough time, virtually all tumors will recur, resulting in the death of the patient. For anaplastic astrocytomas, the 1 year survival is about 70% and the 5-year survival rate about 20%. For glioblastomas, the 1-year survival is about 45%, and the 5-year survival is less than 5%.

In general, after initial surgery we actively recruit patients into treatment studies with new forms of chemotherapy. This is followed by conventional radiation after which the majority of patients have a disease free interval of between a few months and a year. The tumor then usually recurs locally (at the site where it was originally diagnosed) at which time additional surgery or salvage chemotherapy is considered. The response rate from this second round of treatment is limited and patients thereafter either deteriorate neurologically or develop fatal pulmonary complications, such as pneumonia or pulmonary embolus, due to limited mobility.

SUMMARY

Primary malignant brain tumors are among the most difficult human malignancies to manage. Other common tumors such as in the lung or breast generally can be cured if caught at an early stage. A 2 cm adenocarcinoma in the peripheral lung field without mediastinal or systemic metastasis can be cured. A small breast carcinoma which has not invaded into the regional lymph nodes can generally be removed with the expectation of permanent control. However, a 1 cm glioblastoma in the anterior right frontal lobe, even with gross total resection and maximum adjunctive radiation, will recur and cause death within a year or two. There is no realistic possibility of cure or even long-term survival.

These patients pose unusual management problems. They require different medications such as anticonvulsants and steroids. There are neurocognitive problems and the quality of life is usually worse than for the other common malignancies. They require a multidisciplinary approach with health care providers skilled in a variety of disciplines.

Malignant gliomas have two components. There is the main bulk of the tumor (the ring enhancing portion seen on the MRI) and the infiltrating portion than cannot be seen by any imaging method. Local control has improved over the past ten years, but control of the infiltrating portion is still lacking. It is likely that some form of biologic approach will be needed to seek out and kill these infiltrating cells that travel with such ease within the white matter tracts of the brain. Perhaps selective delivery of self-destruct genes to these cells will be possible. Perhaps the search and destroy potential of the immune system can be harnessed. If so, this incurable cancer may some day be brought under control. The effort involved will be extensive both in the laboratory and in the clinic.

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Concepts and Controversies in the Treatment of Brain Metastases

Prakash B. Chougule, MD

Brain metastases commonly occur in patients with cancer and present clinical treatment dilemmas to the radiation oncologist, medical oncologist, neurosurgeon, neurologist and primary care physician alike. Lung, breast, melanoma, colo-rectal and renal cell carcinoma constitute over 90% of the metastases seen. The frequencies of brain metastasis range from 9-45% of patients with cancer and vary depending on the site and histology of the primary cancer and methods used for diagnosis.[1] These frequencies are increasing, perhaps due in part to the increase in the incidence of diagnosis of lung and breast cancer. Improvements in brain imaging and increased time of survival of cancer patients due to multimodal treatment of the primary cancer may also be partly responsible for the increased incidence of brain metastases. The autopsy incidence of brain metastasis is reported to be as high as 45% (Table 1) . The treatment decision is quite often challenging. The typical patient reaction is of loss of control of life and physical function and a sense of demise. The physician's approach to this problem is typically dictated by the functional status of the patient, emotional desires and needs, estimated duration of life, probability of the return of neurologic deficits and time-benefit ratio.

Brain metastases are unique in that they occur within closed skull cavity, causing increased intracranial pressure and sometimes cerebral herniations. Since there are no lymphatics in the brain, there is poor drainage of edema. The brain tissue does not regenerate, so permanent, nonreversible signs are frequent. The most common symptoms are headache, focal weakness, behavioral or mental status change and seizures. Occasionally ataxia, aphasia or other vague symptoms may occur. The most common signs are hemiparesis, impaired cognitive function and motor or sensory loss leading to weakness. Approximately 65% of patients have symptoms that have occurred within the previous three months. The caring physician's awareness and high index of suspicion of brain metastasis is therefore very important, particularly when a patient is known to have had a history of cancer. Two thirds of metastases occur in the frontal/parietal lobes of the brain; the remaining one third occur in the temporal, cerebellar and occipital lobes. A majority of patients have multiple brain metastases, although 30% have a solitary lesion. CT scan of the head with and without contrast is generally the first test leading to the diagnosis of brain metastasis. In fact, a CT scan is routinely done as a base line study to rule out metastasis in a majority of patients diagnosed with lung, breast, gastro-intestinal and renal malignancies. This could preclude a surgical procedure for the primary tumor. A base line CT scan is warranted in most patients with melanoma due to the increased incidence of this condition and the resulting increase in brain metastases.[2] Although CT scan identifies most metastatic tumors over half a centimeter in size, MRI is superior in the detection of smaller lesions.[3]

ABBREVIATIONS USED

CT	Computed tomography
GK	Gamma Knife
MRI	Magnetic resonance imaging
RTOG	Radiation Therapy Oncology Group
TID	ter in die [L.], three times a day
WBRT	Whole brain radiotherapy
XRT	X-ray therapy

TREATMENT

Treatment for brain metastasis should be based on the following criteria:

1. Neurological performance status
2. Stage, histopathology and status of the primary tumor
3. Number of metastatic lesions in the brain
4. Presence or absence of other systemic disease, and
5. Estimated probability of survival from primary cancer.

A. MEDICAL TREATMENT

Steroids: Corticosteroid administration can result in symptom improvement in 60-75% of the patients with brain metastasis.[4] Corticosteroids decrease the permeability of tumor capillaries to small hydrophilic molecules and can diminish or prevent acute increases in tumor capillary permeability that might otherwise caused by cranial irradiation,[5] Although the types of glucocorticoid administered for this purpose do not differ greatly in effect, use of dexamethasone (16 mg in divided doses) has been common. Higher doses can be employed if no improvement occurs.[6] Steroids are generally started at diagnosis or 24 hours prior to the beginning of radiotherapy, then tapered and discontinued upon the completion of radiation. Steroids are helpful primarily in the amelioration of symptoms through reduction of edema and a possible oncolytic effect. The palliative benefit of steroids is short-lived, with a possible improvement in the median survival from one month without to two months with treatment.[4]

Anticonvulsants: Fifteen to 20% of patients with brain metastasis present with seizures; an additional 10% develop seizures eventually. Dilantin is commonly used in the dosage of 100 mg tid.[4,7,9] Prophylactic use of anti-convulsants is not recommended due to its side effects. Besides, in a study by Cohen the incidence of seizure in patients who received prophylactic dilantin was reported to be identical to that patients who did not.[9]

Chemotherapy: Chemotherapy is not commonly used for treatment of brain metastasis. Hidalgo et al. reported the use of simultaneous radiotherapy Cisplatin in a pilot study of 13 patients showing a relatively high (53.8%) complete response rate, but long term results are unknown.[10]

B. Radiotherapy

Whole brain radiotherapy (WBRT) has been the mainstay in the treatment of brain metastasis since the 1950's; palliation is achieved in 60-80% of patients.[1,11-13] However, local control of the disease in the brain can be achieved only in approximately 50% of patients while additional brain metastasis develop in 20%. The evolution of fractionated radiotherapy has largely been attributable to the knowledge gained from the Radiation Therapy Oncology Group (RTOG) studies.[7,14,15] In these studies different treatment schedules of radiation doses did not appear to vary either median survival or local and distant tumor control rates. Currently the most accepted treatment schedule for WBRT is 3000 cGy in ten fractions. The functional response to radiotherapy is seen in 50-60% of patients regardless of the dose schedule. The median survival is 3-6 months with a one year survival of 15%. Re-irradiation after initial treatment of brain metastasis with WBRT in selected patients reportedly shows 42% symptomatic improvement. Unfortunately the median survival of five months and the potential increased morbidity precludes the use of reirradiation of the whole brain in most cases.[16]

The side effects of whole brain radiotherapy are generally acceptable, with major complications reported in less than 3% of patients receiving a tumor dose in excess of 4000 cGy. Late side effects generally occur after six months and can manifest as diminished intelligence, hypothalamic dysfunction and behavioral and cognitive impairment. Morbidity is higher in patients receiving hypofractionated (300-600 cGy per fraction) than in patients who receive protracted radiotherapy schedules.[17] Radiation induced changes increase significantly with increasing age.[20]

> *The physician's approach to the problem of brain metastases is typically dictated by the functional status of the patient, emotional desires and needs, estimated duration of life, probability of the return of neurological deficits, and time-benefit ratio.*

◆

C. Surgery

Surgery is generally contraindicated in patients with multiple cerebral metastases and in patients who have extensive or disseminated extracerebral disease. A subset of patients with brain metastasis do benefit from surgical resection of metastasis followed by radiotherapy. Survival is further improved with surgery and WBRT in patients with breast and renal cell carcinoma. Surgery is generally recommended for patients who have an undetectable primary {5-20%}, patients with severe neurological disability from the metastasis, patients with stable or controlled primary cancer, and patients who have recurrence of brain metastasis following radiotherapy.[3,7,14] Unfortunately only 25% of patients are surgical candidates.[11]

Surgery is almost always followed by radiotherapy. In a study of 85 patients at the Mayo Clinic, Smalley et al reported a recurrence rate of 85% vs. 21% in favor of the radiotherapy.[11] Systemic failure in patients remaining disease free from the brain metastasis was higher in the adjuvant group. Thus for patients with favorable manifestations such as a solitary brain metastasis that is resectable, controlled or stable primary cancer and good performance status, survival is improved.[21-24] Patchell and Mendell have shown significantly better median survival (16 months vs 4 months) with surgery plus WBRT than with WBRT alone.[25-26] Intracranial relapse was the cause of death in 9% of the patients with surgery plus WBRT vs 50% with WBRT alone.[26] Improvement in overall survival, quality of life and functional independence and reduction of recurrence at the site of original metastasis were all observed in the surgery plus WBRT group.

D. Radiosurgery or Gamma Knife Surgery

Although surgery followed by whole brain radiotherapy offers the best treatment results, only 25% of patients are eligible for surgery in most centers. A

Table 1
Autopsy Incidence in Cancer Patients

Series	Number of Cases	Intracranial Metastases Number	Intracranial Metastases Percentage
Willis 1979	461	23	5
Lesse & Netsky 1954	595	207	35
Earle 1954	710	79	10*
Chason et al. 1963	1,399	167	12*
Aronson et al. 1964	2,406	397	16.5*
Posner et al. 1978	2,375	572	25
		467	20*

*Dural metastasis not included

Table 2
Randomized Treatment of Brain Metastasis with Gamma Knife Radiosurgery, Whole Brain Radiotherapy or Both

R
E — Whole brain radiotherapy (WBXRT)-30 Gy in 10 Fx's
G
I — Gamma Knife (GK)-30 Gy to the margin
S
T — Gamma Knife (GK)-20 Gy to the margin and WBXRT 30 Gy in 10 Fx's
E
R

Eligibility:
1. Confirmed diagnosis of cancer (lymphomas, small cell lung ca excluded)
2. Age ≥ 18
3. Karnofsky performance status ≥ 60.
4. Minimum expected survival of 3 months.
5. A baseline MRI of the brain.
6. ≤ 3 metastatic lesions.
7. The target volume of each metastatic lesion ≤ 30 cu cm.
8. No previous radiation or surgery.

single metastasis occurs in 30-50% of patients and 83% have three or fewer metastatic tumors.[27] Furthermore, there is no clear correlation between the number of cerebral metastases and systemic spread of malignant disease. Many patients could benefit from palliative treatment and hope for potential long term survival if treatment alternatives with a lower risk and results equal to or better than those of surgery could be offered. Preliminary results indicate that radiosurgery using Gamma Knife or linear accelerators offers such an alternative.[28, 30]

Gamma Knife or linear accelerator radiosurgery has been used ‘â?H <‘safely in the management of brain tumors.[28-34] Radiosurgery offers delivery of a very high dose of radiation in a single treatment session and can be done on an outpatient basis. The treatment is effectively restricted to the pathology to be treated, thus sparing normal brain tissue from high dose radiation. Gamma Knife technology uses 201 cobalt 60 sources focusing on a single point. The radiation dose can be targeted around the lesion with an accuracy of 1 mm or less. The technology and the technique have been described elsewhere.

Brain metastases are usually well circumscribed and more or less spherical lesions, which makes them appropriate targets for radiosurgery.[35] More patients are eligible for radiosurgery than open surgery since most metastatic lesions can be treated radiosurgically, but not all can be addressed with open surgical techniques. There are also fewer medical contraindications to the use of the radiosurgery, since it avoids general anesthesia and the stresses associated with open surgery. The experience with the Gamma Knife for treatment of brain metastasis at the Karolinska Institute showed a local tumor control rate of 94% in a series of 160 patients.

Since the Gamma Knife addresses only the lesions treated, there is a 15-30% risk of new metastatic lesions occurring in the remaining (untreated) areas of the brain . Whether the addition of WBRT to radiosurgery would be beneficial is currently unknown, since there have been no prospective studies. Because WBRT with or without surgery has been a standard treatment, it is important to study the benefits of radiosurgery with or without WBRT and WBRT alone. A randomized three-arm study is currently ongoing within the Clinical Oncology Group at Brown University (a multihospital trial: Dr. Chougule-Principal Investigator) for patients with ≤3 metastatic lesions (Table 2). The randomization is between Gamma Knife radiosurgery alone (GK) vs. whole brain radiotherapy alone (WBRT) vs. both (GK +WBRT). The hypothesis is that radiosurgery alone is better than or equal to standard open surgery with WBRT and that the addition of WBRT may not be necessary in this patient subgroup with ≤3 metastatic lesions. If this turns out to be true, significant morbidity from open surgery can be avoided and these patients can be more effectively treated, with the efficacy of local control from Gamma Knife Radiosurgery exceeding 90% as compared to 40-50% from whole brain radiotherapy. Patients who have 4 or more lesions, however, carry a significantly higher risk of additional metastasis in the brain for which

Gamma Knife Radiosurgery seems less feasible; whole brain radiotherapy is therefore recommended for this group. A baseline MRI is obtained to detect smaller lesions that may be missed on CT scans. A quality of life analysis is also being carried out in this ongoing trial.

In summary, the treatment of brain metastasis remains a challenging issue. Although palliation is the main objective in a majority of the patients with brain metastasis, improvement in survival and quality of life can be achieved in several types of patients who have favorable manifestations.

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Treating the Chronic Pain of Cancerous CNS Tumors

Gerhard M. Friehs, MD

Divinum (est) sedare dolorem [it is divine to relieve pain].

Despite substantial progress in the pain control capability of modern medicine, most patients with cancer still experience significant amounts of pain at some point during the course of their disease[1] The most common reason for this pain is undertreatment. Effective treatment of cancer pain has become an increasingly important issue since survival rates with even the worst cancer forms have increased dramatically in recent years because of improved therapeutic regimens. Although the mainstay of pain treatment is pharmacological therapy, a few patients require more aggressive methods in order to control the pain enough to assure adequate quality of life. These more invasive procedures are often ablative or destructive in nature.

Neurosurgical treatment of pain has a long and colorful history. The first real pain control procedure was performed in 1912 by Spiller and Martin when they interrupted the major pain-conducting fiber system in the spinal cord, the spinothalamic tract.[2] The procedure became well known as a cordotomy several decades later. Destruction of pain-related systems in the brain was dependent on the development of stereotactic neurosurgery. First used by Zernov in Moscow in 1889, stereotactic neurosurgery was refined by Horsley and Clarke around 1908 for animals and by Spiegel and Wycis in 1949 for human use.[3] Since then, neurosurgical procedures for the treatment of chronic cancer pain have been repeated and refined in many ways but the old principles still hold true. Today, with the advent of modern analgesic therapy, neurosurgical treatment for cancer pain is necessary only on rare occasions.

This discussion focusses first on possible mechanisms of CNS cancer pain production, then outlines general guidelines and neurosurgical techniques for the treatment of cancer pain before reviewing the selection criteria for possible candidates for neurosurgical cancer pain treatment, and concluding with an overview of common treatment options available to neurosurgeons involved in pain treatment.

Mechanisms of Cancer Pain

The central nervous system (CNS) in strict anatomical terms consists of the brain proper and the spinal cord. It is responsible for the transmission and perception of pain. The CNS itself, however, is only rarely the origin of pain, although cancer pain related to CNS malignancies is possible. Table 1 summarizes pain syndromes associated with CNS cancer.

For intracranial or intracerebral cancerous tumors, headache is the most common presenting syndrome. Headache can be either specific for tumor location [such as retro-orbital headaches for orbital location as described in detail elsewhere] or rather inspecific.[4] The overall prevalence of headaches in patients with CNS malignancies is 60-90%; it is even higher in patients with cancer of the posterior fossa. When the tumor mass involves or compresses the dura, meningeal headaches may result. The same is true for leptomeningeal seeding of certain intracerebral cancer types, predominantly metastatic leptomeningiosis or glioblastoma with leptomeningeal involvement.

Cranial nerves may also be affected by skull base tumors or by processes located around the brain stem. Compression syndromes for the trigeminal or the glossopharyngeal nerve are most common and also result in the most severe neuralgic pain which is often refractory to pharmacological treatment. Thalamic pain syndrome is very rare and is caused by specific destruction in the thalamic sensory nuclei. Compression syndromes may also result when cancer encroaches upon the vertebral column or its contents. Although relatively infrequent, pure epidural compression is associated with specific neurological deficits and pain. Epidural compression is most often accompanied by a radicular component caused by nerve root compression. When the leptomeninges are affected, the same holds true as for intracranial processes: seeding of primary or secondary malignant tumor cells into the spinal meninges is rare but typically followed by severe pain. Tumor spread into the spinal cord proper is also possible. In addition to various neurological deficits, intramedullary tumors such as metastases or gliomas can produce pain which would then be referred to as central pain syndrome.

Although strictly speaking, the various plexopathies and peripheral neuropathies are not diseases of the central nervous system, they nevertheless bear mention in any comprehensive discussion of cancer-related pain. Cervical and lumbosacral tumors or malignancies in the axilla are responsible for nerve plexus pain which often has both nociceptive and neuropathic components. The causes of peripheral neuropathy range from direct compression syndromes to demyelinating processes such as paraneoplastic peripheral neuropathy.

The mechanism of pain syndromes elicited by CNS cancer can, therefore, be categorized as: a) compression of intracranial or intravertebral contents (i.e. headaches, radicular pain), b) irritation of cerebral or spinal meninges (i.e. leptomeningeal carcinomatosa), or

Abbreviations Used

AA	Anaplastic astrocytoma
ACTH	Adrenocorticotrophic hormone
CNS	Central nervous system
MAC	Monitored anesthesia care
MRI	Magnetic resonance imaging
NSAID	Non-steroidal anti-inflammatory drug
WHO	World Health Organization

c) lesions within central systems (i.e. thalamic pain syndrome).

TERMINOLOGY

For purposes of treatment, there are three basic types of pain: nociceptive pain (sometimes called somatic pain), neuropathic pain (sometimes called deafferentation pain), and idiopathic pain. It is important to distinguish the three types because both origin and therapy differ significantly between them.

The terms "nociceptive" and "somatic" refer to pain elicited by ongoing stimulation of primary afferent neurons (nociceptors). These receptors have been identified in various tissues such as skin, muscle, connective tissue, and viscera.[5] The pain is described as sharp-throbbing or deep-cramping when associated with visceral involvement. Representative of this type is pain caused by leptomeningeal seeding of cancer or bone pain. In contrast, neuropathic pain is believed to be caused by aberrant somatosensory information and is described as an unusual, unfamiliar pain.[6] It can be associated with either the central or the peripheral nervous system and is also associated with injury or irritation to the nerves themselves. Examples of this type of pain include brachial plexopathy in breast cancer with axillary lymph node enlargement or the thalamic pain syndrome. Pain of CNS cancer frequently cannot be interpreted as purely nociceptive or neuropathic; combinations of these types are the general rule. If the pain is neither nociceptive nor neuropathic or if the suffering is out of relationship to the morphology causing pain, the term idiopathic pain is often used. Since idiopathic pain is not typically seen in cancer patients, it will not be discussed here.

TREATMENT OF CHOICE: GENERAL PRINCIPLES

Any treatment of CNS cancer pain should be directed first towards removing the cause of pain. Compression syndromes can be corrected by decompressing the intracranial or intraspinal tumor mass through a surgical approach or with radiotherapy. Sometimes rather extensive procedures are necessary in order to achieve adequate decompression. For example, when the bulk of a tumor is located anterior to the spinal cord, only a vertebral corpectomy or vertebrectomy may suffice. For leptomeningeal disease, treatment consists of intrathecal chemotherapy, radiotherapy, or a combination of both. The irritation on the meninges caused by cancer cells is reduced and patients experience pain relief within days after initiation of treatment. Only in cases where therapy is not possible and pain prevails should treatment be directed primarily towards the symptom (pain) rather than the origin (cancer) in an attempt to maintain high quality of life.

> *The most common reason for pain caused by cancerous CNS tumors is undertreatment.*

The mainstay of treatment for CNS cancer pain is pharmacological therapy. According to recommendations issued by the Word Health Organization in 1990, a stepwise approach should be considered.[7] Table 2 depicts this analgesic ladder. First-stage therapy consists of a combination of non-steroidal anti-inflammatory drugs (NSAID) with or without an adjuvant. The term "adjuvant" refers to medication that is neither an analgesic nor an NSAID. Typical adjuvants include antidepressants (amitriptyline), anxiolytics or tranquilizers (benzodiazepines) and anti-epileptic membrane stabilizers (i.e. carbamazepine or phenytoin). Should this regimen fail, mild to moderately strong opioids such as codeine are added to the therapy. If this second step does not relieve the pain, stronger opioids including morphine or fentanyl are included. The preferred routes of administration are non-invasive, *i.e.* oral, transmucosal, or transdermal. With severe cases of cancer pain, however, continuous intravenous or subcutaneous infusions may be necessary for adequate relief. About 70-90% of patients will experience sufficient pain relief with these WHO guidelines leaving 10-30% of cancer pain patients with continuing pain for whom neurosurgical pain management can be considered.[8]

NEUROSURGICAL PROCEDURES

I) Interrupting transmission

a) Percutaneous or Open Cordotomy

Originally performed with an open surgical approach by Spiller and Martin in 1912 and Forster in 1913, open cordotomy used to be one of the most powerful and successful operations for neurosurgical pain control.[2,9] Several decades later the technique was further refined to allow for a minimally invasive percutaneous operation of low morbidity and mortality.[10,11] The functional element of cordotomies is destruction of the spinothalamic tract, which is the main pain conducting pathway, in the anterolateral quadrant of the spinal cord, contralateral to the painful area.

Today, percutaneous or open cordotomy is recommended only for cancer pain patients with a life expectancy of less than 12 months who have nociceptive pain (preferably unilateral lower extremity pain) limited to one side of the body below the level of the clavicle. For such patients, the immediate post-operative pain relief rate of about 90% drops to about 55% after one year.[12] Mortality is very limited (0-5%) and morbidity is usually transient, with ipsilateral paresis and bladder dysfunction being the most common side effects (3-10%). The proper pain-abolishing effect of cordotomies may be accompanied by contralateral loss of temperature sensation.[13] Patients must be educated about this possible untoward effect in order to prevent inadvertent thermal injury to the treated body side.

The open approach necessitates a laminectomy typically of T1 under general anesthesia. After opening of the dura and direct exposure of the spinal cord, the anterolateral quadrant is visualized anterior to the dentate ligament and transsected at a depth of 4-5mm with a special cordotomy knife.

Local anesthesia with anesthesiological monitoring (MAC - monitored anesthesia care) is sufficient for the percutaneous route. The C 1-2 interspace is most often chosen as the entry point for a spinal needle that is inserted into the intrathecal space. After positive return of cerebrospinal fluid, a small amount of water-soluble contrast media is injected. With the

Table 1
Pain Syndromes Associated with CNS Cancer

- Cranial Origin
  - intracerebral tumors
    - headaches
    - cranial neuralgias
      - trigeminal neuralgia
      - glossopharyngeal neuralgia
    - central pain syndrome
  - leptomeningeal tumors
    - leptomeningeal irritation pain
    - headaches
  - bone tumors
    - skull base tumors
      - orbital syndrome
      - parasellar syndrome
      - middle cranial fossa syndrome
      - jugular foramen syndrome
      - clivus syndrome
      - sphenoid sinus syndrome
    - skull tumors
      - leptomeningeal irritation pain
      - bone pain

- Spinal Origin
  - vertebral tumors
    - axo-atlanto-occipital tumors
      - occipital pain
      - neck pain
    - vertebral tumors
      - brain pain
      - epidural compression syndrome
      - back pain
      - radicular pain
      - cauda equina syndrome
    - leptomeningeal tumors
      - leptomeningeal irritation pain
    - spinal cord (intramedullary) tumors
      - central pain syndrome

- Other Origin
  - cervical, brachial, lumbo-sacral plexopathy
    - neurogenic pain
  - peripheral neuropathy
    - neurogenic pain

help of an image intensifier the dentate ligament can be visualized indirectly and a radiofrequency needle placed anterior to it about 4-5 mm into the spinal cord. The correct position of the needle is neurophysiologically verified by testing with stimulation at low frequencies (2 Hz) for inadvertent ipsilateral motor responses and at high frequencies (50 Hz) for contralateral sensory responses. A lesion is then made by heating the needle to 60-70 û Celsius for 10-20 seconds. Next is contralateral testing for motor function and pain relief, followed by the increasing of the time that the needle is tested and repeated testing until the desired pain relief is achieved or adverse effects occur.

b) Mesencephalic Tractotomy

Mesencephalic tractotomy can be viewed as an extension of a cordotomy into the mesencephalon. The targets are the spinothalamic tract and more medially the reticulothalamic tract at the level of the tectal plate. The procedure was originally described by Wycis and Spiegel in 1962 and is indicated for cancer patients with pain in the head, face, neck, and upper extremities.[14] While nociceptive pain responds particularly well to this operation, promising results have also been reported for neuropathic pain .[15,16]

Mesencephalic tractotomy can be carried out under local anesthesia and requires stereotactic guidance. After application of the stereotactic frame and completion of magnetic resonance images (MRI), the target points are calculated. A temperature-controlled radiofrequency probe is then inserted through a small burrhole contralateral to the painful area and advanced to the target point. Stimulation verifies the correct position neurophysiologically before the lesioning procedure is performed. Due to the anatomical proximity of the superior and inferior colliculi, gaze disturbance is the most common side effect, occurring in 10-20% of patients.[3] In addition, the medial lemniscus can be affected, resulting in contralateral dysesthesias (5-15%).

c) Trigeminal Rhizotomy

Branches of the trigeminal nerve can be irritated or compressed by CNS cancerous tumors. Metastases to the skull base or nasopharyngeal carcinomas infiltrating through the skull base can precipitate isolated trigeminal neuralgia. This neuropathic pain has responded well to a percutaneous procedure more commonly employed for trigeminal neuralgia of non-malignant origin (tic doloreux). In this procedure, the ganglion of the trigeminal nerve, the Gasserian ganglion is lesioned through the foramen ovale. After application of local anesthetic and sedation, an insulated needle is inserted through the skin of the cheek underneath the zygoma into the foramen ovale under fluoroscopic guidance.

Table 2
Sequential Approach to Cancer Pain Management (WHO 1986, 1990)

pain	–	STEP 1: non-opioid ± adjuvant
if pain persists	–	STEP 2: opioid for mild to moderate pain + non-opioid ± adjuvant
if pain persists	–	STEP 3: opioid for moderate to severe pain + non-opioid ± adjuvant

Electrical stimulation can be used to evoke paresthesias in the region of the face ipsilaterally. Lesioning of the ganglion should be performed with generous analgesia and sedation. Pain relief is immediate and usually lasts for several years.[17] Trigeminal rhizotomy, also called gangliolysis, has no associated mortality and less than 1% serious morbidity.

II) Modulating Transmission

a) Spinal Intrathecal or Intraventricular Morphine

Application of morphine into the spinal subarachnoid or intraventricular space must be considered for pain patients who have failed stage three of the WHO recommendations. Tremendous doses of parenteral or enteral morphine reaching toxic levels (respiratory depression) or uncontrollable side effects at relatively low doses (ileus, hallucinations) are also indications for subarachnoid administration. [18] Good initial response to opioids is a good prognostic factor.

Studies on receptor populations in brain and spinal cord tissue suggest that the spinal application and the intraventricular route are not interchangeable.[19,20] Intractable pain in the head and neck area is less likely to respond to spinal intrathecal morphine than to intraventricular morphine. Secondly, patients who fail test injections of spinal intrathecal morphine may still be candidates for the intraventricular application. Spinal intrathecal morphine is delivered through a continuous infusion pump via an intrathecal catheter. The procedure can be performed in MAC with a Touhy-type needle passing the catheter into the intrathecal space. The pump itself is implanted into a subcutaneous pouch in the abdomen inferior to the rib cage. Refill of the pump can be done percutaneously on an outpatient basis and should be scheduled at least every 90 days. It has been shown that implantation of this rather costly device is economically feasible if the estimated survival of cancer patients exceeds 3 months.[33]

Implantation of an intraventricular catheter is done under local anesthesia through a small burrhole typically on the right frontal bone just posterior to the hairline (Figure 1). This catheter can be attached to a continuous infusion pump or, more easily, to a small subcutaneous reservoir (OMMAYA reservoir) which holds a volume of about 1 ml. Daily filling of the reservoir is required and can be done either by the patient or by a relative.

The advantages of subarachnoid (whether spinal intrathecal or intraventricular) morphine are multiple. Typically, the dose necessary for 24 hours of pain relief is only a minute fraction of what would be required with parenteral or enteral forms and ranges from 0.5 mg - 10 mg per 24 hours. The risks of implantation are minimal and limited to infection at the implantation site. Although intrathecal morphine is known to produce respiratory depression even as late as 24 hours after injection, this complication, due to unknown protective mechanisms, does not typically occur in patients with cancer.

b) Stimulation (neuroaugmentative procedures)

Continuous stimulation of the dorsal columns of the spinal cord, the somatosensory thalamic nuclei, and the periaqueductal or the periventricular gray has been shown to reduce pain effectively. However, these procedures are not typically performed on patients with cancer-related pain and are therefore not discussed in detail here. The interested reader is referred to the relevant literature.[21,22]

III) Modulating Perception: Surgery of the limbic system

a) Medial Thalamotomy
b) Cingulotomy
c) Anterior Capsulotomy

All procedures of the limbic systems require stereotactic equipment including a stereotactic frame, a stereotactic imaging study (MRI, CT; rarely ventriculography as well) and a thermal radiofrequency probe. With refined stereotactic techniques the mortality rate is reduced to 1% or less; general complications such as infections or hemorrhages are also rare. The goal of surgery in the limbic system is to reduce suffering (the affective component related to pain). Thus, after limbic surgery painful stimuli are still transmitted to cerebral centers, but are no longer perceived as painful.

Medial thalamotomy was first described by Mark et al. in 1960.[23] In this procedure, the medial thalamic nuclear group and the intralaminar nuclei contralateral to the painful area are destroyed with one or more lesions. These nuclei receive projections from pain receptors and in turn project to areas of the limbic striatum. Bilateral procedures are possible but increase the risk of side effects. Specific complications include contralateral paresthesias and memory disturbance. The success rate in a recent literature review was quoted as 60-80% for prolonged periods of time.[24]

In the initial 1962 report, Foltz and White described the cingular gyrus which connects the medial-frontal cortex, anterior thalamic nuclei, and

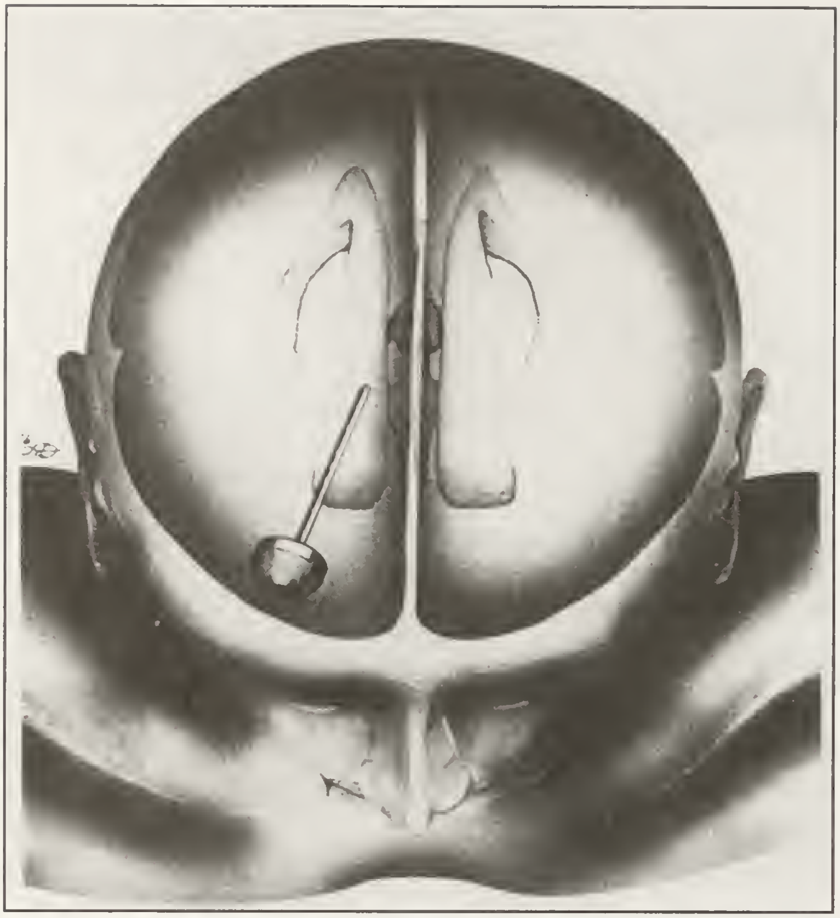

Figure 1. Placement of an intraventricular reservoir (OMMAYA) is depicted. The reservoir is connected to a catheter which is inserted into the right frontal horn of the lateral ventricle. After subcutaneous implantation the reservoir can be accessed through the skin and refilled.

intralaminar thalamic nuclei with the hippocampus formation.[25] Bilateral interruption of the cingulum has been shown to be effective in painful disorders particularly when a component of anxiety or depression coexists. The procedure is very safe and usually does not cause any measurable side effects. Pain relief can be expected in 50-75% of cancer patients.[26]

Anterior capsulotomy is a variation of a leucotomy (functional disconnection of the frontal lobes) in which the anterior limbs of the internal capsule are surgically interrupted as they pass between the head of the caudate nucleus and the putamen. The first leucotomy was described in 1937.[27] Although the original technique had a high success rate, the associated complications were intolerable. Changes in personality and behavior were common. Refinement of the technique and limitation of the surgical procedure to the small area of the anterior internal capsule have created a safe procedure with limited side effects.

IV) Reducing Pain by Unknown Mechanisms

Hypophysectomy

First reported in 1953, hypophysectomy today is performed in three different ways. [28] A percutaneous transnasal transsphenoidal approach with stereotactic guidance can be used for thermal ablation of the pituitary gland. Another method involves placing a needle into the subarachnoid space around the pituitary in order to instill alcohol, which denatures the pituitary gland. Thirdly, an open transnasal or sublabial, transsphenoidal approach can be used for surgical removal of the pituitary gland. It was originally believed that hypophysectomy was effective only for hormone dependent cancer, but it has since been shown to be effective also in relieving the pain of tumors other than prostate or breast cancer. With all three techniques, pain relief can be expected in up to 90% of patients.[29,30] Mortality is possible but unlikely and usually occurs after alcohol injection. Side effects are rare. Possible mechanisms underlying the function of hypophysectomy include increased hormone release (ACTH), neuropeptide release (beta-endorphine) or hypothalamic injury.

V) Gamma Knife Radiosurgery for Pain

A new technique that can be considered a viable alternative to the invasive procedures described above is now available for treatment of intracranial pain. Instead of using thermo-coupled radiofrequency electrodes to create a lesion at a specific place, the Gamma Knife can be used for the same purpose. With its array of 201 Cobalt-60 sources assembled in a spherical fashion, the Gamma Knife can create highly focussed lesions as small as 4mm in diameter. The advantage of the Gamma Knife lesioning procedure is that it is performed through the closed skull; its disadvantage is that it requires approximately one month for the radiation-induced lesion to form and for the pain relief to begin. Gamma Knife procedures successfully performed for treatment of cancer related CNS pain have included medial thalamotomy, cingulotomy, anterior capsulotomy, hypophysectomy, and trigeminal rhizotomy.[31,32,33]

SELECTION OF PATIENTS

Although pain management for patients with cancer must be tailored to each individual case, there are some general guidelines on how patients should be matched to the appropriate treatment.

1) Causal must be chosen over symptomatic therapy although even causal therapy is often only palliative. Thus patients with compression syndromes should be considered for surgical - radio - or chemotherapy in order to reduce tumor mass and alleviate compression. In most cases of leptomeningeal cancer spread, it is unnecessary to consider aggressive neurosurgical pain management since causal treatment - intrathecal chemotherapy - effectively abolishes both the cause and the concomitant symptom.

2) Only if patients fail causal therapy or present with contraindications to it should aggressive

(i.e. neurosurgical) pain management be considered.

3) Non-invasive pharmacological therapy is the mainstay of treatment. If this fails, less rather than more invasive neurosurgical treatment is preferable and more peripheral surgical approaches are preferable to central ablative procedures. It is important to point out to the patient that more invasive treatment is not necessarily more effective and might be associated with greater side effects, since patients sometimes feel that optimal treatment is withheld if a medial thalamotomy or cingulotomy is not offered to them on the first visit.

4) Nociceptive pain typically responds well to morphine while neuropathic pain generally does not. The focus in patients with nociceptive pain should therefore be to maximize opioid therapy and, if necessary, consider intrathecal or intraventricular application. Patients with neuropathic pain may respond to alternative pharmacological therapy. If these measures fail, central procedures that alter pain perception are advisable.

5) The timing of invasive neurosurgical procedures is crucial. Unfortunately, it happens all too often that patients are referred for ablative procedures after having suffered from intractable pain for months. If pharmacological therapy fails, neurosurgical therapy is the next best strategy. Waiting should not be an option, especially for patients who have only a limited amount of time left.

6) It cannot be overemphasized that pain is a multimodal disease of multimodalities and as such requires an interdisciplinary approach for successful control. The pain management team should include primary care physicians, neurosurgeons, related neurological specialists, anesthesiologists, psychologists, and rehabilitation specialists.

CONCLUSION

Modern neurosurgery offers a variety of treatment options to patients with painful CNS cancer tumors. When indicated, these procedures should be performed early in the course of the disease. The procedures are ablative in nature and usually minimally invasive. Mortality is low and side effects are mostly transient with little or no severe morbidity. The success rate ranges from 90% immediate relief to about 50% relief at one year postoperatively. With the introduction of Gamma Knife radiosurgery, it is now possible to perform intracerebral ablative procedures without penetrating the skull at all, thereby avoiding operative risks. Although the experience with radiosurgical pain treatment is limited, preliminary results are promising.

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New Modalities in Treating Pituitary Adenomas

Ivor Jackson, MD and James V. Hennessey, MD

Pituitary adenomas account for approximately 15% of all intracranial tumors.[1] They are almost always benign, though malignant tumors with distant metastases do occur rarely. Pituitary tumors are either functioning or non-functioning depending on whether the cell of origin secretes a hormone that produces an endocrine hypersecretory syndrome. Management of a pituitary adenoma depends on its size and possible encroachment upon vital structures, especially the optic chiasm, as well as its effects on endocrine function. In this review, we will discuss the approach to treatment of pituitary tumors with particular reference to some of the newer modalities available.

CLINICAL MANIFESTATIONS

Depending on the population investigated, up to 70% of pituitary adenomas may show clinical and/or biochemical evidence of hypersecretion.[1,2] Prolactin (PRL) is the hypersecreted hormone in 30-40% of all resected tumors.[3] Hyperprolactinemia gives rise to the clinical syndrome of galactorrhea-amenorrhea in females or to hypogonadism in males. Although tumors secreting the gonadotropins, follicle stimulating hormone (FSH) and luteinizing hormone (LH) or the a subunit, account for 10-20% of secretory adenomas, clinically they usually behave as if they were non-functioning tumors.[4] Adenomas secreting adrenocorticotropic hormone (ACTH) give rise to Cushing's Disease and account for 2-10% in different series, while growth hormone (GH) secreting tumors (2-17%) cause acromegaly.[5] Tumors secreting thyroid stimulating hormone (TSH) may cause thyrotoxicosis. They are however, rare and contribute no more than 1% of all pituitary adenomas.[5] Secretory pituitary tumors may rarely be associated with endocrine tumors in the parathyroid or pancreas, as part of the multiple endocrine neoplasia type I syndrome (MEN I), or with the McCune-Albright Syndrome of polyostotic fibrous dysplasia, pigmented skin lesions and sexual precocity.[5]

> *Management of a pituitary adenoma depends on its size and possible encroachment upon vital structures, especially the optic chiasm, as well as its effects on endocrine function.*

Non-secreting pituitary adenomas constitute a large proportion of pituitary macroadenomas (tumors greater than 1cm in size). They present with a picture of hypopituitarism and neurologic manifestations which include headache and visual field abnormalities.[4,5]

ABBREVIATIONS USED

ACTH	Adrenocorticotropic hormone
CSF	Cerebrospinal fluid
DDAVP	Deamino D-Arginine vasopressin
FDA	Food & Drug Administration
FSH	Follicle stimulating hormone
GH	Growth hormone
IGF-1	Insulin like growth factor 1
LAR	Long acting release
LH	Luteninizing hormone
MEN	Multiple endocrine neoplasia syndrome
MRI	Magnetic resonance imaging
PRL	Prolactin
TSH	Thyroid stimulating hormone

DIAGNOSIS

The diagnosis of pituitary tumors requires a high index of clinical suspicion. Patients with galactorrhea - amenorrhea and serum PRL levels above 200 ng/ml almost certainly have a prolactinoma though a lower level does not rule out a tumor. The diagnosis of acromegaly is frequently overlooked despite the presence of the classical features which include enlarging hands and feet, prognathism and coarsening of the facial features, accompanied by headache and excess perspiration.[6] Such patients have an elevated serum GH and insulin like growth factor 1 (IGF-1) or somatomedin C. In normal subjects, the serum GH is suppressed under 2 ng/ml following a glucose load in contrast to acromegaly where there is either no suppression or a paradoxic increase. Patients with Cushing's Disease caused by a pituitary adenoma secreting ACTH, generally have features of glucocorticoid excess. A useful screening test is an overnight dexamethasone suppression test with decadron 1 mg at midnight.[7] Patients with Cushing's Disease do not show the normal suppression of their serum cortisol and plasma ACTH at 9:00 a.m. Following identification of pituitary hyperfunction imaging of the pituitary should be undertaken by means of magnetic resonance imaging (MRI) with gadolinium enhancement. In patients with secretory pituitary tumors who have microadenomas (hypodense on MRI), the rest of the anterior pituitary function is likely to be intact. However, macroadenomas (which show enhanced density on MRI) are associated with varying degrees of hypopituitarism. Patients with non-functional tumors most commonly present with headaches or visual field abnormalities and the tumor is often discovered on brain imaging as an "incidentaloma".[3] Such patients often have varying degrees of hypopituitarism and it is therefore critical to evaluate the adrenal and thyroid

Table 1
Treatment of Pituitary Tumors

- Surgery
    - Transsphenoidal Adenomectomy
    - Subfrontal Craniotomy
- Radiation
    - Conventional Supervoltage Radiotherapy
- Stereotactic Radiosurgery
    - Gamma Knife
- Pharmacologic Agents
    - Dopaminergic Agonists
        - Bromocriptine
        - Pergolide
    - Somatostatin Analogues
        - Octerotide
        - Octerotide-LAR

axes in such patients. Some patients with non-secreting tumors have no complaints of any headaches but present with amenorrhea (females) or diminished libido (males) and on investigation are found to have hypogonadotropic-hypogonadism.[4]

TREATMENT

Surgery. Transsphenoidal surgery with selective adenomectomy is the treatment of choice for secretory tumors which are microadenomas.[8] In such cases, an immediate cure can be obtained by a skilled surgeon in over 70% of cases. Suprasellar extension and cavernous sinus invasion markedly limit the probabilities of cure with preservation of intact anterior pituitary function. Nevertheless, surgical decompression is worthwhile especially if there is tumor encroachment of the optic chiasm, characteristically causing a bitemporal hemianopsia. In some cases, especially those with extension of tumor into the brain, a transcranial/subfrontal approach may allow the surgeon to gain better access to the tumor and achieve significant debulking. The mortality rate is very low with the transsphenoidal procedure (under 1%), but may rise to 3-4% with the transcranial approach. With transsphenoidal surgery, the complications include transient diabetes insipidus, which may occur in up to 25% cases and satisfactorily responds to fluid adjustment and/or desmopressin (DDAVP) 1-2 μg (0.25 - 0.5 ml) given subcutaneously usually once or twice daily.[9] Other complications include cerebrospinal fluid (CSF) rhinorrhea, meningitis and wound infection which are observed in less than 4% cases. Hypopituitarism as a complication of transsphenoidal surgery is influenced by the adequacy of pituitary function pre-operatively as well as the extent of the surgical resection. The necessity of continuing glucocorticoid replacement is determined by measuring an AM serum cortisol after stopping glucocorticoids for 24-48 hours. Simultaneously, other components of pituitary function may be monitored.

Radiation Therapy. Pituitary tumors can be treated with conventional super voltage radiotherapy delivered to the pituitary by a linear accelerator in which 4,000 to 5,000 rads (40-50 gray) are given as fractional doses of 180 rads per day, 5 days per week over a 5-6 week period.[10] Such treatment is often considered for patients with significant tumor mass or persistent hypersecretion especially acromegaly, following surgery. The disadvantage of this treatment for secretory tumors is the slow onset of therapeutic effect, for example in acromegaly there is a 50% reduction in GH levels after two years and 75% after five years--and the high incidence of anterior pituitary failure. Complications of the radiotherapy include cranial nerve damage, cerebral radionecrosis and cognitive defects.

Stereotactic Radiosurgery. Most recently stereotactic radiosurgery (Gamma Knife Therapy) has been introduced for the treatment of pituitary tumors.[11] This involves the delivery, in a single session, of a high dose of ionizing radiation (cobalt-60) as precise narrow collimated beams through multiple ports. Since the dose gradient is very steep, surrounding tissues receive minimal irradiation. The resulting lesion is sharply circumscribed and the rest of the pituitary may receive little radiation. The limiting factor to the dose of radiation administered is the proximity of the tumor to the optic chiasm. The role of gamma knife therapy as a primary or secondary treatment of pituitary tumors is currently under investigation; this treatment modality has a number of advantages over conventional radiotherapy including absence of significant irradiation of surrounding brain tissue. It is our current practice to utilize gamma knife therapy rather than conventional radiotherapy when radiation treatment is being considered for pituitary tumors.

MEDICAL THERAPY

Dopaminergic Agonists. Bromocriptine (Parlodel), a dopaminergic agonist, is the treatment of choice for prolactinomas.[12] It produces suppression of the serum PRL as well as shrinkage of the tumor mass, often with a dose of only 2.5 mg twice/day (Fig 1). In some patients, however, the side effects of nausea, constipation, nasal stuffiness, dizziness and digital vasospasm can be intolerable (Fig 2). Taking the medication with food and gradually increasing the dose by no more than 1.25 mg every 3-4 days improves tolerance for the medication. As an alternative, Pergolide (Permax) may be used, and it is sometimes better tolerated than Bromocriptine. However, it is not approved by the Food and Drug Administration (FDA) for treatment of pituitary tumors. Dopaminergic agonists provide benefit in approximately 10-15% of cases of acromegaly, usually

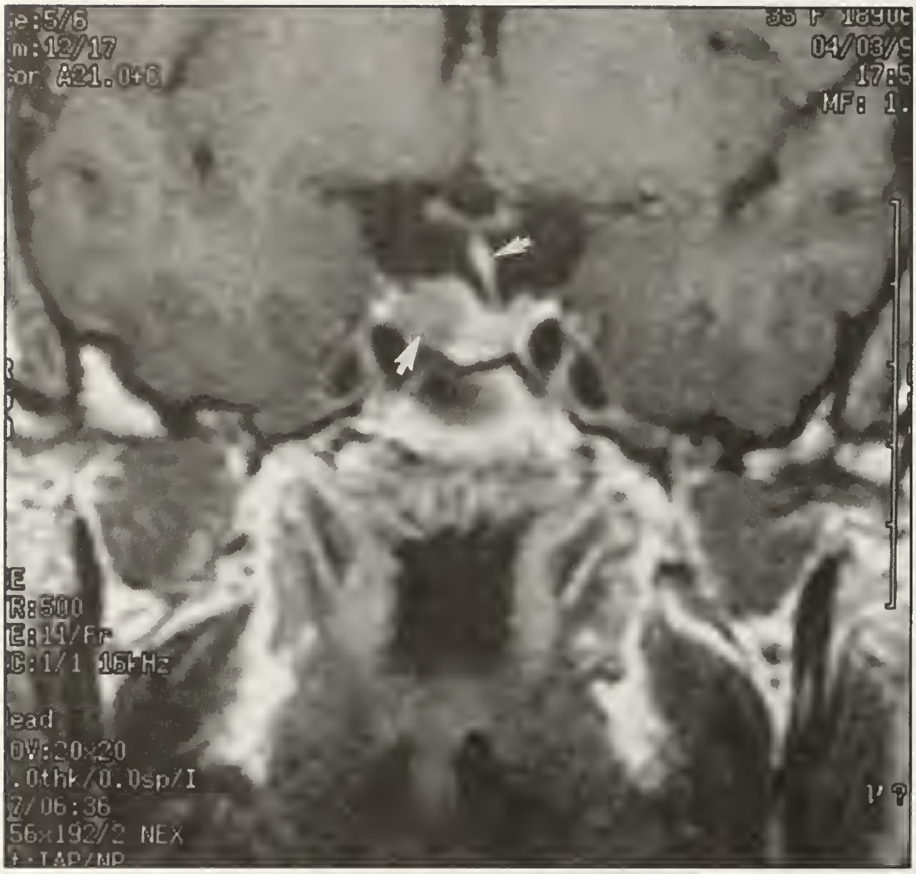
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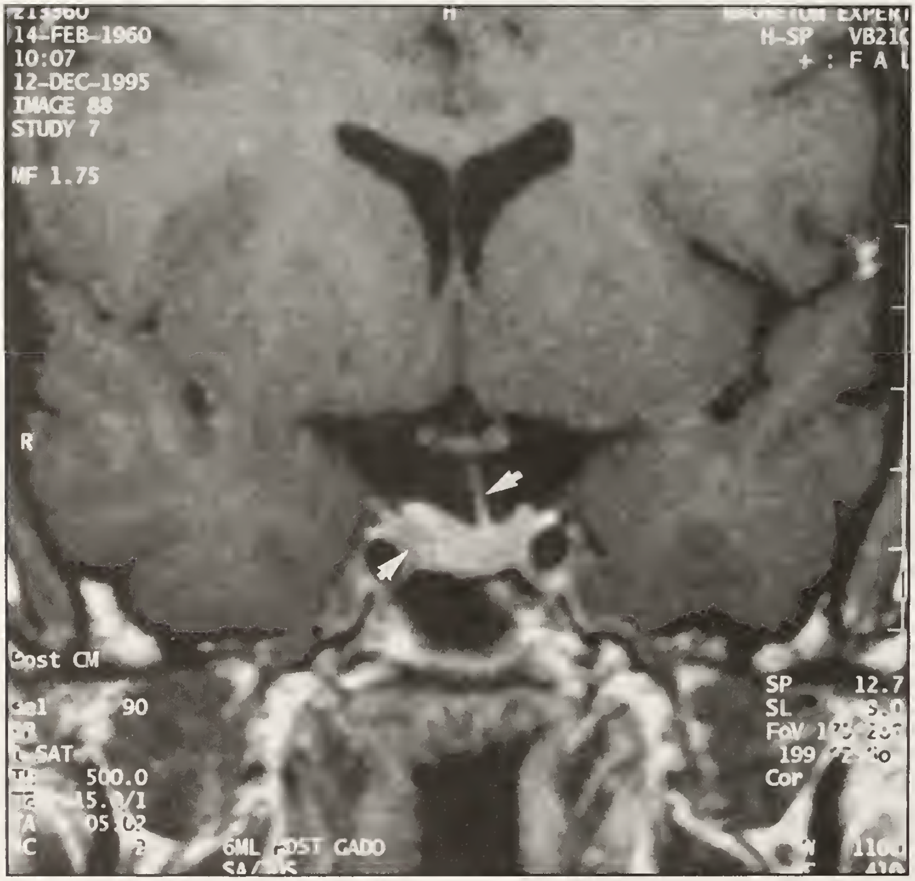
Fig 1
a) MRI (coronal view) of the pituitary of a 32-year-old female with galactorrhea - amenorrhea and a serum PRL of 222 ng/ml showing a 9mm microadenoma (lower arrow) which is hypodense following gadolinium. Note shift of the stalk to the left (upper arrow).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10:07
12-DEC-1995
IMAGE 88
STUDY 7
MF 1.75
R
Post CM
6ML POST GADO
SP 12.7
Cor

b) Following treatment with bromocriptine, the right sided microadenoma has diminished in size to about 6mm (lower arrow), associated with a serum PRL of 23 ng/ml. The microadenoma is not as clearly defined as before following gadolinium. However, the stalk is still shifted to the left (upper arrow).

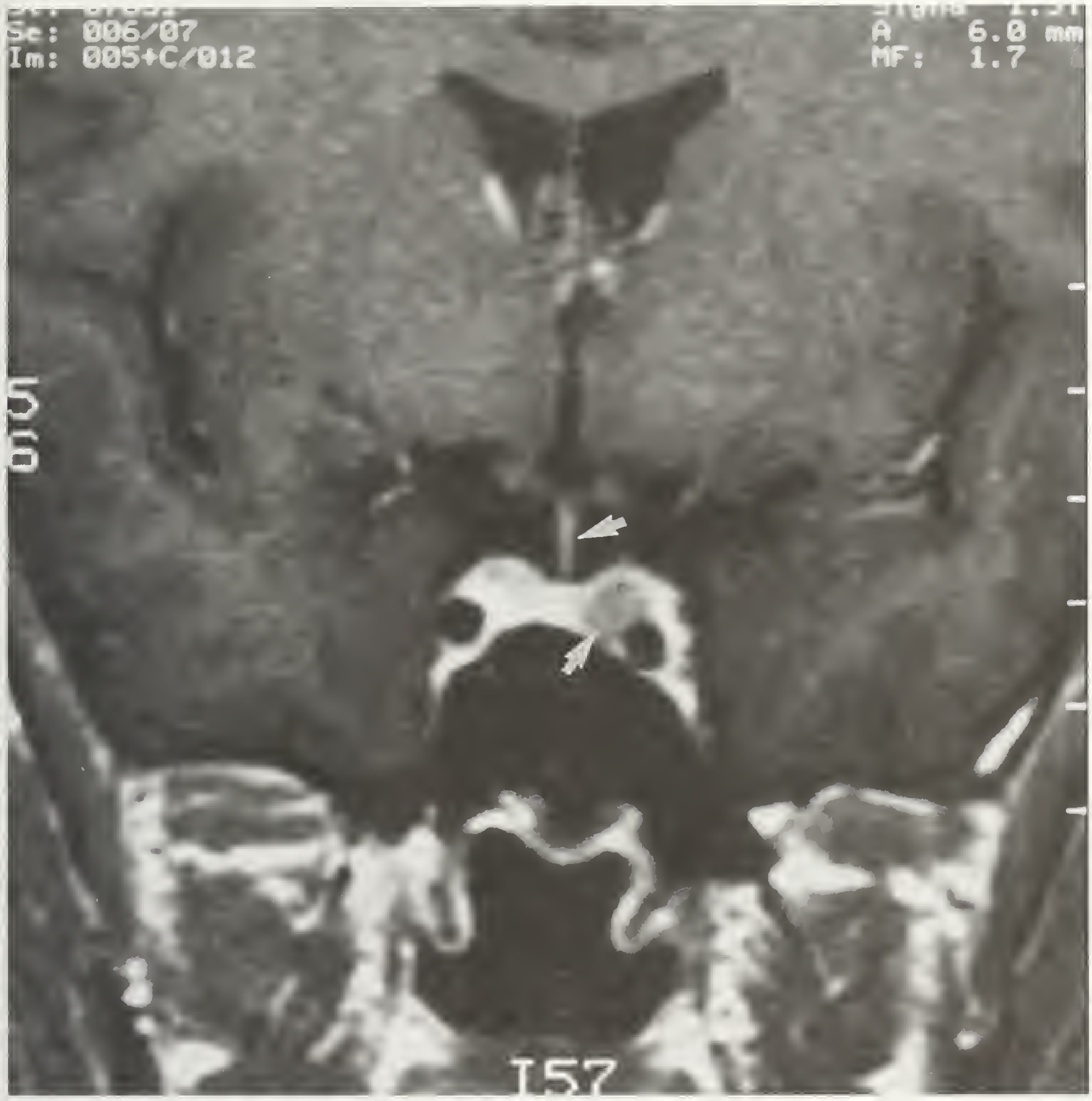

Fig 2
MRI (coronal view) of the pituitary of a 42-year old female with galactorrhea-amenorrhea and a serum PRL of 146 ng/ml. The pituitary gland is normal in height. There is a 6 mm focus of decreased enhancement following gadolinium on the left side of the pituitary (lower arrow) just medial to the patent internal carotid artery (black). The pituitary stalk (upper arrow) is not deviated. This patient has not tolerated dopaminergic agonists. This microadenoma would be suitable for either gamma knife therapy or transsphenoidal surgery.

the milder forms, but rarely produce significant reduction in tumor size.[13] Doses up to 20 mg/day are generally required.

Somatostatin Analogues. The medical management of acromegaly has been revolutionized by the development of long acting analogues of somatostatin.[5,13] The octapeptide analogue (Octreotide; Sandostatin) given by subcutaneous injection in doses of 100-250 µg 2-4 times daily is effective in normalizing GH and IGF-1 levels in about 50% of acromegalics. In a further 40% of cases clinical and/or biochemical improvement is seen (Fig 3). Pituitary tumor size is reduced by 20-30% on MRI in around 70% of patients. The major side effect of concern is the development of gall stones in about 20% cases.[14] Octreotide has also been beneficial in the treatment of TSH secreting tumors.

Most recently a depot long-acting somatostatin analog (sandostatin LAR) has been prepared.[15] It is a formulation that incorporates octreotide in microspheres of a biodegradable polymer and is administered by injection once per month. It has been shown to be effective in maintaining suppressed GH levels in acromegalic subjects. It is likely to be several years before it is available and approved by the FDA for treatment of acromegaly. The various modalities available for treatment of pituitary tumors are summarized in Table 1.

CONCLUSIONS

A number of different approaches to the management of pituitary tumors are now available. These involve transsphenoidal adenomectomy, transcranial resection, stereotactic radiosurgery, supervoltage radiotherapy and various pharmacologic agents. The ideal treatment in the individual case is best tailored by a team involving the combined skills of the neuroendocrinologist, neurosurgeon, radiotherapist, neuroradiologist and neuropathologist.

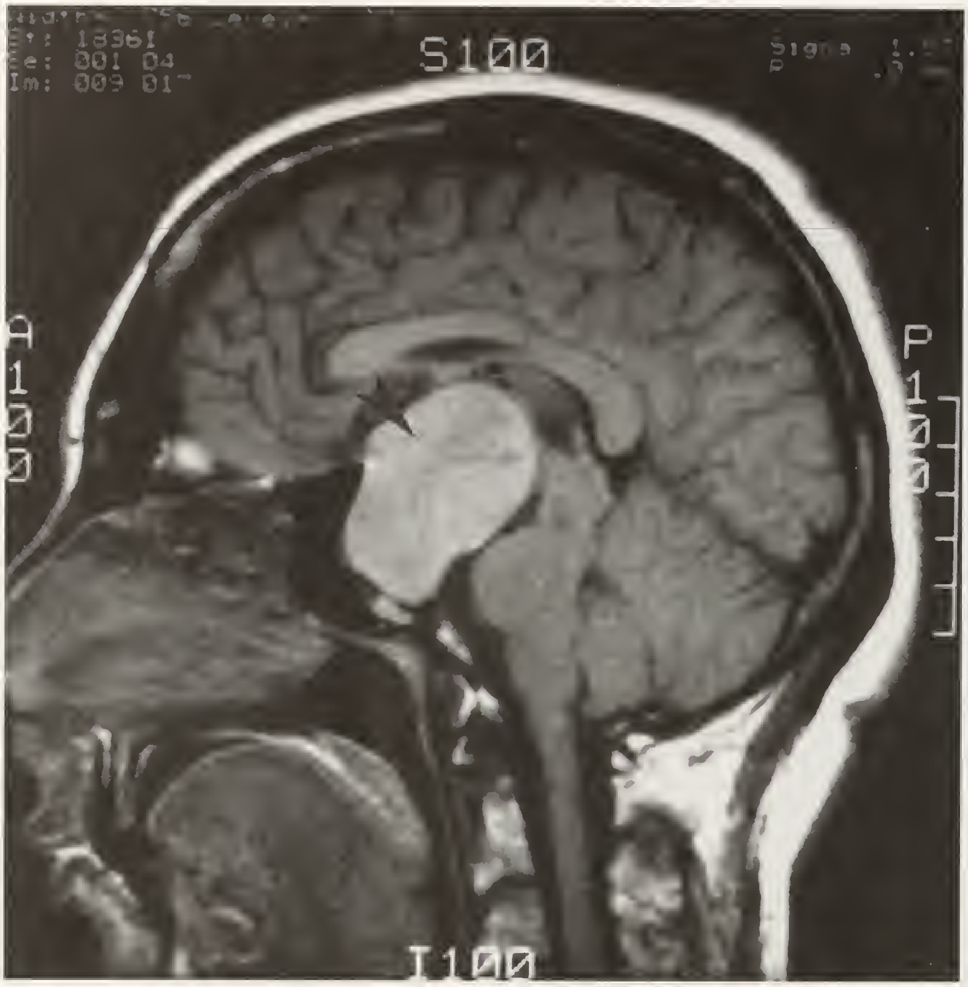

Fig 3
MRI (sagittal view) of pituitary in a 32-year-old patient with acromegaly. There is a huge sellar mass (5.5 cm in diameter) extending superiorly to the right subfrontal region and diencephalon, and inferiorly through the sella turcica. The patient had bitemporal hemianopsia. The tumor could not be surgically resected and it is too big for gamma knife therapy. Treatment with the somatostatin analogue octreotide has been given with some reduction in GH levels but little change in tumor size.

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Brain Tumors of Childhood

John A. Duncan III, MD, PhD

In children, brain tumors are the second most common neoplasm. They are responsible for 20% of all cancer in children and for 20% of childhood cancer deaths.[1] The annual incidence ranges from 2-3 tumors per 100,000 children, resulting in about 1700 new cases per year in the United States.[2] At a children's hospital such as Hasbro, 50 - 100 children who have or had brain tumor will be actively followed or are being treated at any given time.

The three most common brain tumors of childhood are medulloblastoma, astrocytoma and ependymoma. Fifty-five to 60% of pediatric brain tumors arise in the posterior fossa and thus will be the focus of this article. Common locations include the cerebellar hemispheres, fourth ventricle, vermis and brain stem. Most children present with signs and symptoms of increased intracranial pressure. These symptoms include headache, nausea, vomiting, lethargy and general irritability. Associated signs are papilledema, head tilt and sixth nerve palsy. This usual constellation of findings is due to a non-communicating hydrocephalus that occurs secondary to obstruction of cerebrospinal fluid (CSF) at the fourth ventricle. Other presenting signs and symptoms occur because of direct compression or invasion of adjacent neural structures. These include lower cranial nerve palsy, motor weakness, ataxia, vertigo, nystagmus and other long tract signs. These findings are less common, but when present suggest brain stem involvement.

Today, pre-operative placement of a shunt is rarely required. Even children with severe hydrocephalus respond to high dose intravenous steroids and stabilize neurologically for 48 to 72 hours. This time window allows the surgeon to complete the pre-operative workup, obtain all necessary radiographic studies and plan for elective surgery. CSF diversion can be performed at surgery if needed. Several complications can be avoided if a CSF shunt is not placed before tumor removal. These include upward herniation and brainstem compression, as well as intraneoplastic hemorrhage and post-operative subdural hematoma formation.[3]

POSTERIOR FOSSA TUMORS OF CHILDHOOD

1. Medulloblastoma

Primitive neuroectodermal tumors found in the fourth ventricle are known as medulloblastoma. These tumors usually arise from the inferior medullary velum and project into the fourth ventricle. They can grow to considerable size prior to diagnosis, often spread cephalad toward the tentorial hiatus. They often invade the brain stem. Ten to 15% can arise in a cerebellar hemisphere without gross connection to the fourth ventricle. CSF spread through the neuroaxis does occur, requiring early radiographic staging of disease.

A non-contrast head computerized tomography (CT) scan shows a midline high density posterior fossa mass that strongly enhances with contrast. Head and complete spine MRIs are required for surgical planning and accurate pre-operative staging. CSF cytology, although usually obtained perioperatively, is of questionable prognostic value. Myelograms for staging are rarely used today.

ABBREVIATIONS USED

CCG	Children's Cancer Group
CCNU	Chloroethylchlorohexylnitrosourea
CSF	Cerebrospinal fluid
CT	Computed tomography
JPA	Juvenile pilocystic astrocytoma
MRI	Magnetic resonance imaging

In general, children under the age of three with radiographic evidence of metastatic disease have a significantly worse prognosis than older children with tumor isolated to the posterior fossa. Because medulloblastoma is considered to be radiosensitive, treatment consists of surgery and irradiation to the entire neuroaxis. Most children over age three receive 54 -60 Gy to the posterior fossa, 34-36 Gy to the remainder of the brain and 24-36 Gy to the spine. Children three and younger usually do not receive radiation therapy because of well accepted deleterious effects to the developing brain.

The goals of posterior fossa surgery are: one, to establish a histologic diagnosis; two, reduce tumor volume, and three, re-establish normal CSF flow. Although controversial, recent CCG study 921 suggests improved survival in children with complete or near total resection (>90%) compared to biopsy alone or partial resection.[4] The importance of this data is that it suggests that near complete resection is beneficial. Aggressive surgical resection of a small amount of residual tumor in eloquent regions (i.e. brain stem) carries unjustifiably high risk for little or no gain.

All children five years and older, require postoperative craniospinal irradiation. Based upon age, residual tumor volume, degree of invasion and metastasis, children are classified into standard or high risk groups (table 1).

Children are high risk even if only one high risk factor is present. These children are treated with chemotherapy, in addition to surgery and craniospinal irradiation. Recent data supports five year survival of 76% in children treated with chemotherapy compared to irradiation alone, representing a marked improvement in high risk patients.[5] Packer reported a 2-year disease-free survival of 96% in children with high risk disease treated with irradiation plus chloroethylchlorohexylnitrosourea (CCNU), cisplatin and vincristine.[6] Even in babies less than 36 months, the results with chemotherapy alone or with reduced dose irradiation are better than expected. In one recent series, 10 of 28 children were alive and free of disease at a median of 150 months after diagnosis. All children in this group who had no metastatic disease outside the posterior fossa were alive and free of recurrence.[7] Chemotherapy has clearly increased survival rates and possibly cured some children with medulloblastoma. Unfortunately, treatment of recurrent disease remains dismal with the likelihood of cure less than 5%. Novel treatments such ablative chemotherapy and stem cell rescue are now being tried at a few centers.

2. Astrocytomas

Cerebellar astrocytomas are most commonly juvenile pilocystic astrocytomas (JPA). Whether solid or partially cystic, these tumors are surgically curable if gross total resection is achieved. The literature supports that 90-94% of patients remain disease free after 20 years![8,9] Post-operative irradiation has never been shown to be effective.[10] Therefore, aggressive surgical resection is required for cure. If the immediate post-operative head scan shows a definite focus of residual tumor, reoperation is indicated even if present in eloquent areas. A referral to more experienced surgeons may be required. If the risks of reoperation in experienced hands is unexpectedly high, stereotaxic radiosurgery (i.e. gamma knife) should be considered. Alternatively, limited field external beam irradiation of 54 Gy is traditionally used for recurrent or residual inoperable tumor, but as stated does not have significant benefit and is not recommended by this author.

Malignant anaplastic astrocytomas or glioblastomas are rare in childhood. They are treated much like supratentorial malignant tumors with surgical debulking, external beam irradiation (up to 60 Gy) and chemotherapy. Again irradiation is held or delayed in children 5 years old or younger. In general, the 2-3 year survival is approximately 50%, with younger (<3 yrs) children faring worse. New therapies with extensive chemotherapy and autologous bone marrow transplantation are currently being tried.

> *At a children's hospital such as Hasbro, 50-100 children who have or had brain tumors will be actively followed or are being treated at any given time.*

Astrocytomas of the brainstem are either focal or diffuse. Diffuse tumors expand an entire region, such as the pons, do not enhance with contrast, are considered malignant and make up the majority of brainstem gliomas. Histologically these tumors are anaplastic astrocytomas. Rarely is histologic diagnosis necessary, and surgery is not beneficial. These children receive external beam irradiation (fractionated or hyperfractionated) and often chemotherapy. There is no known effective treatment and life expectancy after diagnosis is usually less than 18 months.

Focal brain stem tumors enhance homogeneously with contrast. Histologically these lesions are juvenile pilocystic, fibrillary or protoplasmic low grade astrocytomas. The most common locations are: 1. cervicomedullary, 2. dorsally exophytic into the fourth ventricle, and 3. tectal. These lesions are usually surgically accessible. Many authors believe these tumors regress or stabilize with near total (80 -95%) resection. Most reports are anecdotal but several clinical series continue to show promise. The indolent nature and relatively small number of these tumors make prospective statistical study difficult. And yet, if the surgical morbidity is felt to be low, surgical resection of low grade gliomas has always been considered to be the most efficacious form of treatment.

3. Ependymoma

Ependymomas almost always present in the fourth ventricle and may project unilaterally or bilaterally through the foramen of Lushka, engulfing the lower cranial nerves.[9,10,11] Brain stem invasion frequently occurs. On head CT or MRI scans, these tumor usually project inferiorly into the foramen magnum, often leading to vomiting without headache and/or head tilt. Like medulloblastoma, CSF dissemination does occur and should be identified at the time of diagnosis.

Once considered to be a radiosensitive tumor, irradiation does not cure these children with ependymoma. A review of the literature, as well as 25+ year experience at the Hospital for Sick Children in Toronto, shows survival to be significantly dependent upon the extent of surgical resection. Complete surgical resection offers good probability of cure. Subtotal resection almost invariably leads to recurrence.[11] In 1991, Healy and colleagues showed that 75% of children without residual tumor on immediate postoperative scan had a 5 year survival without progressive disease, compared to a 0% chance of freedom from progressive disease in children with residual tumor after surgery. To date, results with adjuvant chemotherapy have been disappointing and this therapy is usually reserved for treatment of recurrent disease.

Unlike medulloblastoma, this locally invasive, often biologically aggressive tumor must be treated with aggressive surgical resection, even in highly eloquent regions such the brain stem or delicate cranial nerves. Today, debate in pediatric neurosurgery continues with regard to the degree of risk

Table 1

	Standard Risk	**High Risk**
Age	Older than 4 years	Younger than 4 years
Size of Tumor	Change T1-T3a	Change T3b-T4
Extent of Disease	Nondisseminated	Disseminated
Extent of Resection	1.5cm^3 residual	1.5cm^3 residual

of surgical morbidity that should be accepted. New technology such as frameless stereotaxis or the "ISG wand", helps define intraoperative location and allows for aggressive resection with decreased risk to adjacent brain. Gamma knife radiosurgery is also being used in several centers on recurrent tumors. Continued improvement in surgical methodology and ablative technique leads to safer and more complete resection which, for this tumor, is the only effective treatment to date.

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The Gamma Knife and Acoustic Tumors

Georg Norén, MD, PhD

Despite contributions to the development of acoustic neuroma surgery by such giants as Harvey Cushing and Walter Dandy, results in the 1950s and early 1960s were far from satisfactory. Surgical mortality in California in the 1950s was 40%.[1] Dramatic improvement followed the introduction of microsurgical techniques in the 1960s.

In 1951, the Swedish neurosurgeon Lars Leksell developed the idea of having a large number of converging beams of ionizing radiation cross-fire targets in the brain.[2] He coined the term "radiosurgery" to describe this concept, since the method of delivering the radiation differed greatly from that of conventional radiation therapy. Leksell's concept was to replace the electrodes used in functional stereotactic neurosurgery by a bundle of converging beams. He also suggested that radiosurgery was appropriate for the treatment of deep-seated, circumscribed intracranial tumors.

The first radiosurgical device was a 300kV industrial X-ray tube connected to a stereotactic frame that was attached to the patient's head. As the patient was moved, the radiation beam entered the head from different directions, though always aimed at the target point. Two patients with trigeminal neuralgia, among others treated with this early technique, remained completely asymptomatic almost 20 years later.[3]

Initial studies used the proton beam from a synchro-cyclotron. This was a very accurate, high energy source, useful for experimental work, but complicated to run and, according to Leksell, not suitable for routine clinical practice.[4] He also considered the linear accelerator as a source but found it to be too inaccurate at that time.

The first device based on Leksell's innovative concept to be developed for routine clinical use was the prototype Gamma Knife, constructed in 1967-68. The earliest stereotactic radiosurgical procedures were predominantly functional; thalamotomies and hypophysectomies for pain were particularly numerous. These, however, were soon outnumbered by other applications such as pituitary and acoustic tumors and vascular malformations.

When the first acoustic tumor was treated with Gamma Knife radiosurgery (GKR) on June 16, 1969, this represented a line of development parallel to that of microsurgery.[5] Since then, more than 4000 acoustic tumors worldwide have been treated with this technique.

THE GAMMA KNIFE

Although the first "modern" Gamma Knife in the United States was installed in Pittsburgh in 1987, the prototype machine (Gamma Knife No. 1) had in fact been shipped to UCLA in 1980 for use as a research tool. The particular unit installed at Rhode Island Hospital in early 1992 (The New England Gamma Knife Center) was the tenth Gamma Knife in the U.S., the first in the Northeastern part of the country, and the 28th world-wide.

The Gamma Knife is an 18-ton machine with 201 permanently mounted ^{60}Cobalt sources arranged spherically (either in a sector or in five rings depending upon which of two current versions of the Gamma Knife is in use) around the patient's head. These sources constantly emit gamma radiation. The beams become sharply demarcated as they pass through two consecutive sets of tungsten collimators, aiming at the focus. Here, at the point of intersection, the radiation is potentially very powerful, whereas each individual beam, on its way through the skull, is weak and will not cause any detectable biological effects.

One of the most unique features of the Gamma Knife is its high degree of technical accuracy, for it can be aligned to an extreme precision of within less than half a millimeter. Another is the steep gradient at the border of each "shot" of radiation, which allows for the delivery of a high dose of radiation to targets with important sensitive structures located just millimeters away or even adjacent to the target's surface.

A work station for dose planning is an integrated part of the Gamma Knife system. Here a plan for the treatment is created based on the anatomical data obtained from the MRI, CT or angiography images and the neurosurgeon's microanatomical knowledge.

Because of the decay of the isotope (half-life 5.26 years), the time to deliver a certain dose will increase gradually. Consequently, the Gamma Knife needs to be reloaded with an interval of up to two half-lives. Due to the non-invasive nature of GKR, only one or two days are usually required for the treatment.

TREATMENT PARAMETERS

Today's dose plans for tumors and vascular malformations tend to contain an increasing number of isocenters ("shots", average 9, range 1-30 at the New England Gamma Knife Center) of different sizes and different relative weighting; the aim is to create a very tight fit between the target and the configuration of the radiation. The whole radiation dose is delivered during one session. The coordinate values for the different "shots" are set and treated one by one as prescribed by the dose plan. Total time of irradiation is usually 15 to 60 minutes but can on occasion run up to 90 minutes if the shape of the tumor is very irregular, as, for example, in neurofibromatosis 2 (NF2) cases.

Since nothing was known initially about the sensitivity of acoustic neuroma tissue and surrounding neural structures to single dose gamma radia-

ABBREVIATIONS USED

CSF	Cerebrospinal fluid
CT	Computed tomography
GKR	Gamma Knife radiosurgery
MRI	Magnetic resonance imaging
MF2	Neurofibromatosis 2
UCLA	University of California at Los Angeles

tion, a wide range of dose levels was used in the beginning. Dose level varied, during the period 1969 to 1980, from between 2000 and 12,500 cGy maximum dose to the center, and from less than 100 up to 7000 cGy to the periphery of the tumor. From that time forward, it was gradually reduced to 1200 cGy to the periphery with a maximum of 2400-3000 cGy to the center of the tumor. This dose appears to be optimal for acoustic tumors, and has been used consistently since 1989.

Work-up and Follow-up

The work-up for GKR includes clinical evaluation, with particular attention to the 5th, 7th, and 8th nerves, brain stem, and cerebellar function. Diagnostic MRI and hearing tests, with emphasis on tone and speech audiometry, are reviewed. Reflex measurements and brain stem audiometry are frequently helpful in establishing the diagnosis but do not play an important role in preparation for GKR.

Follow-up normally consists of MRI (T2W axials pre-contrast, T1W 3 mm adjacent axials and coronals post-contrast) and tone and speech audiometry at six months and annually thereafter for four to five years. Any follow-up beyond this point will be based on the outcome so far. Clinical assessment is added as necessary.

Results

The results reported here are based on experience from 588 treatments of 530 acoustic tumor patients in Stockholm, Sweden, 1969 through 1994, and 113 treatments of 112 patients in Providence, Rhode Island, 1992 through 1995.

Imaging

The goal of GKR for acoustic tumors is to arrest the growth of the tumor permanently. Ninety-five percent of unilateral acoustic tumors show permanent growth control, most of them shrinkage, following GKR.[6] The earliest detectable change, a decrease of enhancement following contrast injection starting centrally and spreading to the periphery, is seen in at least 70% of the tumors.[7] This process, which reflects the development and propagation of necrosis, usually becomes apparent 6-12 months after GKR and seems to be correlated to permanent growth control.[8] It is observed less frequently in small tumors (≤1 cm intracranial size and intracanalicular), where it does not seem to affect growth control. Temporary swelling of the tumor together with the loss of enhancement is seen in 5-7% of cases.

> *The goal of Gamma Knife radiosurgery is to arrest the growth of the tumor permanently. Ninety-five percent of unilateral acoustic tumors show permanent growth control, most of them shrinkage, following Gamma Knife radiosurgery.*

Since acoustic neuromas are benign tumors with slow cell turn-over, their response to radiation is generally protracted. Although on occasion shrinkage may be detected as early as a few months after treatment (Fig 1), it usually develops over a period of one or more years (Fig 2). One-third of the tumors show shrinkage one year after the treatment, two-thirds four years after the GKR, and just over 90% 10 years after the procedure.[7]

Late recurrences of unilateral tumors (more than 5 years out from radiosurgery) are extremely unlikely if the treatment was adequate. In most cases the treatment can be defined as successful after 1-3 years, especially if there are signs of shrinkage.

Five percent of tumors fail to respond to the treatment which, when this occurs, usually becomes apparent within 2-3 years. If, following GKR, an acoustic tumor has increased in size, at least two years need to elapse before temporary swelling can be differentiated from failure.

Long-term Growth Control

The long-term results are of particular interest in connection with this slow- growing type of tumor and are therefore presented here in some detail.

The very first series of eight unilateral tumors was treated consecutively between 1969 and 1974 with the prototype Gamma Knife.[9] These acoustic neuromas had a maximum intracranial diameter of 1.1 to 3.0 cm (average 1.8 cm). Of the five responding tumors, three showed shrinkage and two remained unchanged for a period of 16.4 to 22.6 years. The minimum radiation dose was on average 1540 cGy (range 200 - 3500 cGy) and the maximum on average 6000 cGy (range 5000 - 10000 cGy). Three tumors did not respond and increased in size following a minimum dose of less than 100 cGy and a maximum of on average 5670 cGy (range 5000 - 7000 cGy). Two of these responded with shrinkage to a second Gamma Knife treatment for a period (to date) of 14.7 and 18.1 years. The third tumor (3.0 cm diameter) was removed two years after GKR.

No patient in this series showed signs of facial neuropathy as a result of GKR, but one did have slight temporary trigeminal dysfunction.

In conclusion, seven out of eight tumors showed permanent growth control with minimal side effects after one or, in two cases, two GKR treatments, giving a total response rate of 88% for an average follow-up time of 17.9 years. It is interesting that the minimum radiation dose in the early cases that responded is very similar to what is used today. The maximum dose was higher but obviously without relevance to the outcome since the non-responding tumors had received the same high maximum dose but a much lower minimum dose.

Facial and Trigeminal Nerves

The incidence of temporary facial weakness or facial numbness induced by GKR treatment is currently less than 2% and approaching 0%. This is in sharp contrast to the 45% incidence of facial neuropathy and 18% of trigeminal dysfunction in 1975 when the minimum dose delivered to the periphery of the acoustic tumors was in the range 2000-7000 cGy.

Cranial neuropathy induced by GKR occurs with a usual latency period of 6-8 months. Onset is sudden and dysfunction lasts from a few weeks if slight to 6-12 months if pronounced.

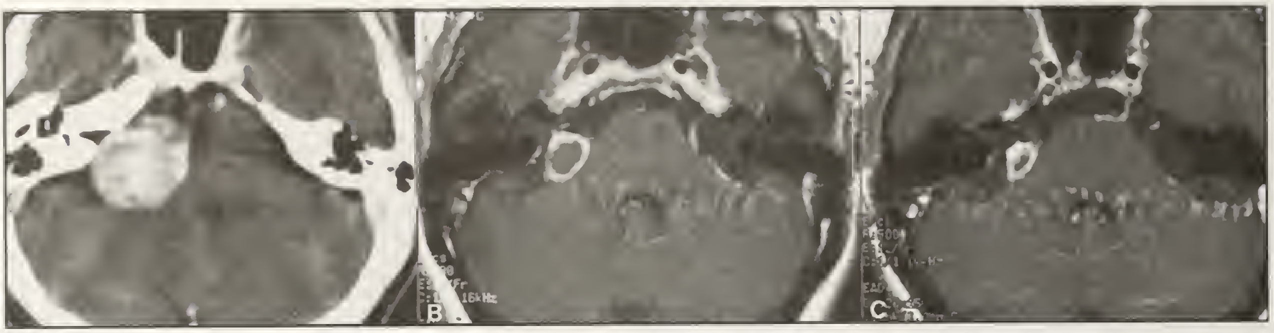

Fig 1. CT (A) and MRI scans (B, C) of 3.0 cm right-sided acoustic neuroma at the time of Gamma Knife radiosurgery (A), and 4 months (B) and 13 months (C) after the treatment. Rapid, marked shrinkage of the tumor with typical finding of necrosis (non-enhancing area B, C). Improved, almost normal hearing in the right ear one and two years after the treatment, pure tone average improved from 18 dB to 10 dB and speech discrimination score went up from 80% to 96%.

Facial weakness always recovers whereas trigeminal neuropathy is less prone to improve especially if pronounced.

HEARING

Hearing present at time of GKR is preserved, either unchanged or nearly so, in 75% of the cases for the first several years. This result, which is based on the experience of the past 5 years, reflects the use of state-of-the-art high resolution MRI imaging, highly accurate dose-planning systems, and optimal choice of radiation dose. Earlier experience suggests the likelihood that this figure might decrease slightly, but it should remain relatively stable in the long-term perspective.[10] Actual improvement of hearing occurs only infrequently (in 1-2% of cases).

CSF CIRCULATION

Impairment of cerebrospinal fluid (CSF) circulation leading to hydrocephalus may occur as a result of mechanical blockage in very large acoustic tumors, while CSF quality changes can be induced by tumors of various sizes. It is also possible that hydrocephalus may also develop following temporary, treatment-induced swelling around the tumor.

Hydrocephalus caused directly by the tumor is seen in 10% of patients; nearly half of these require a shunt before, and the other half at some point after the radiosurgical procedure. Peritumoral swelling giving rise to a blockage of the CSF circulation and requiring a shunt is found in 0.5% of patients.

It is well-known that some acoustic tumors, primarily those of size 2 cm and up and (in our experience) in patients more than 60 years old, tend to induce hydrocephalus spontaneously before they have been treated. The exact reason for this is unclear, but some of these tumors do cause a tenfold or more increase in CSF protein concentration, a factor of known importance in the development of hydrocephalus.

NEUROFIBROMATOSIS 2

The bilateral (NF2) acoustic tumors show a somewhat different behavior as they also do in relation to microsurgery. 85% of these display signs of growth control following GKR. They may, however, recur five or even ten or more years after treatment and, a course that initially appeared successful. The incidence of facial and trigeminal dysfunction following radiosurgery for bilateral is as low as for unilateral tumors. In order to preserve hearing, however, the dose of radiation to the core of the neuroma has to be kept lower because of its different anatomical relationship to the eighth nerve. This lower dose level may at least in part explain the somewhat higher recurrence rate in the NF2 tumors.

DISCUSSION

Most acoustic tumors with a maximum intracranial size of up to 3 cm qualify for Gamma Knife radiosurgery. Except for local unavailability, there are in fact few reasons why Gamma Knife radiosurgery should not be considered instead of microsurgery for the vast majority of acoustic neuroma patients, including young and otherwise healthy individuals.[11] Possible exceptions include:

1) Situations in which there are signs of increased intracranial pressure, and where the choice is between excision of the tumor or radiosurgery plus shunt. The patient's condition, age, and personal preferences will then be of importance for the final decision.

2) Cases of tumors with an intracranial diameter of 2 cm or more and with clinical signs of trigeminal nerve involvement, when, on rare occasions, the facial numbness is so pronounced that it is almost painful. In such situations the trigeminal nerve needs to be decompressed without too much delay and, consequently, excision of the tumor is usually a better choice than radiosurgery.

The fact that the tumor is literally removed following microsurgery but not in radiosurgery is frequently better accepted by the patient than by the surgeon. Such operations have traditionally been defined as successful if the tumor has been radically removed. Other standards are required for evaluation of the results of GKR.

A few issues frequently come up when discussing Gamma Knife treatment of acoustic tumors. One is the risk that the treatment might induce the formation of other tumors in the future. Based on clinical data and experiences as well as theoretical considerations, this risk level is less than one per mille and probably even lower. There is thus no reason to withhold Gamma Knife radiosurgery from young individuals who prefer radiosurgery to microsurgery.

It is sometimes claimed that radiosurgery makes any subsequent microsurgical procedure more difficult because of formation of scar tissue. This seems to be based on experience from a small number of operations undertaken when the tumor has increased in size due to lack of response or temporary swelling. In the latter situation, the surgery is

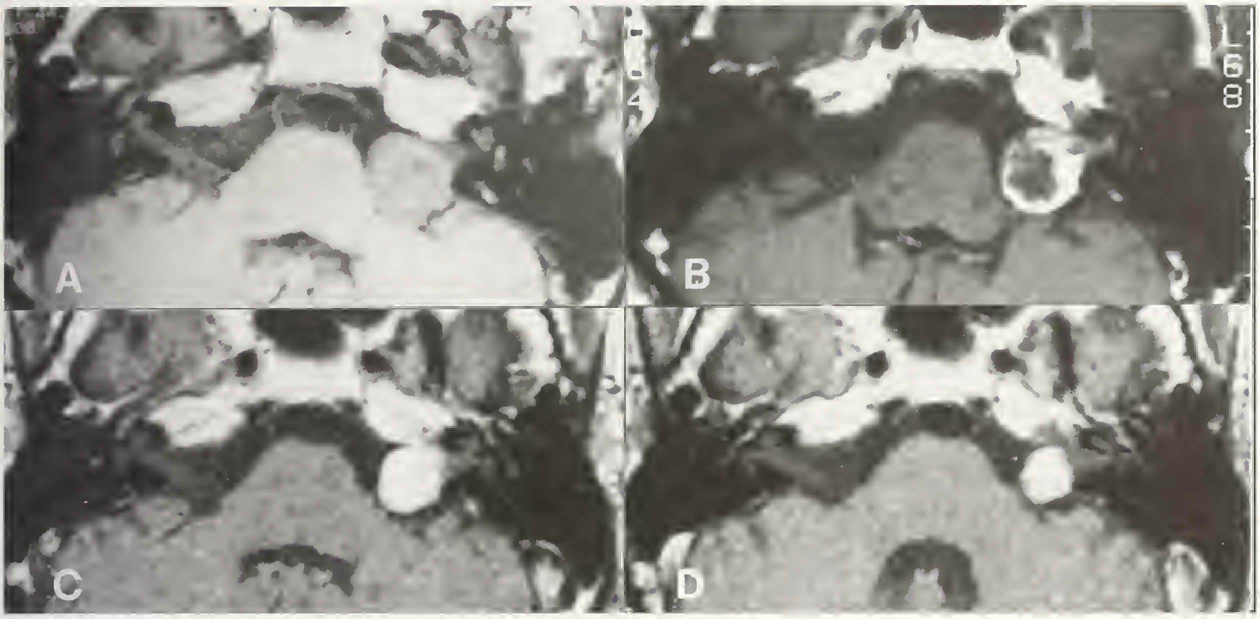

Fig 2. MRI scans of a 1.9 cm left-sided acoustic tumor before (A), and 5 months (B), 12 months (C), and 25 months (D) after Gamma Knife radiosurgery (T1W, Gd-enhanced B-D). Loss of contrast enhancement is the earliest sign after treatment and indicates necrosis (B). Gradual shrinkage is subsequently seen (C,D) to a diameter of 1.4 cm while the contrast enhancement is again more homogeneous, a frequent and normal finding. The radiation dose to the periphery was 1300 cGy, at the center 1900 cGy.

probably more difficult but transient edema in the tumor is not an indication for excision. Whether surgery is more difficult in situations when the tumor has not responded remains to be clarified.

Non-responding acoustic tumors can be treated a second time with Gamma Knife radiosurgery without increased risk other than that of failure to preserve hearing.

Conclusions

Ninety-five percent of unilateral acoustic neuromas treated with GKR show permanent growth control after the treatment. Non-responding unilateral tumors show up within five years, and recurrences beyond that are extremely unlikely. There is no risk of intracranial bleeding, infection or CSF leak as a consequence of the treatment. Disturbance, usually temporary, of the facial and trigeminal nerve function occurs following less than 2% of the procedures. A majority of the patients retain unchanged hearing for several years. Even medically infirm patients can undergo this treatment since the overall risks are low. All acoustic neuromas with an intracranial tumor size of up to approximately 3 cm, with few exceptions, are suitable for GKR.

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Public Health Briefings

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Judith Feldman, MD, MPH, and John P. Fulton, PhD

Vancomycin Resistant Enterococci

Utpala Bandy, MD, PhD

Utpala Bandy, MD, MPH, is State Epidemiologist and Chief, Communicable Diseases, Rhode Island Department of Health.

The emergence of drug-resistant microorganisms is increasingly recognized as a major public health threat. This article will deal with the threat posed by an emerging class of nosocomial infection for which little or no effective antimicrobial therapy is available, namely, enterococci which have developed resistance to vancomycin (VRE). Just as penicillin resistant staphylococci emerged as important nosocomial pathogens in the 60's and 70's, and methicillin resistant *staphylococcus aureus* was the scourge of the 80's, VRE has become the infection control practitioner's buzzword for the 1990's.

EPIDEMIOLOGY

Inappropriate use of vancomycin in the hospital and home health setting has contributed to the selective survival of innately resistant organisms with subsequent overgrowth and colonization in the intestinal tracts of certain populations, including critically ill patients or those with underlying disease or immunosuppression (ICU and oncology patients), persons who have had an intra-abdominal or cardio-thoracic surgical procedure or an indwelling urinary or central venous catheter, and persons who have had a prolonged hospital stay or received multiantimicrobial or vancomycin therapy.

According to the National Nosocomial Infection Surveillance System (NNISS), the proportion of nosocomial infections due to Enterococci rose between 1986 and 1989 to 12%, second only to *E. coli*. The first cases of disease attributable to VRE were reported in 1988. From 1989 to 1993, the percentage of NNISS enterococcal isolates resistant to vancomycin increased overall from 0.3% to 7.9%, and the percentage of enterococcal isolates from intensive care units that were resistant to vancomycin increased from 0.8% to 14%, representing a 34 fold increase! The occurrence of VRE in NNISS hospitals was associated with larger hospital size (>200 beds) and university affiliation. The actual increase is probably greater because the fully automated methods used in many laboratories cannot consistently detect vancomycin resistance, especially moderate resistance.

Enterococci are part of the normal flora of the intestinal and vaginal tracts. Most people are colonized with the species *E. faecalis*, while about 25% are colonized with *E. faecium*. There are 10 other species known to cause disease. Enterococci are not particularly virulent, but in patients with other serious medical problems, enterococcal infections can be deadly. The mortality from enterococcal bacteremia ranges from 34% to 46%. Most infections are attributable to the patients' own flora. Increasingly, however, VRE infections are nosocomially acquired indirectly, by transient carriage on the hands of health care workers, or by contaminated environmental surfaces and patient-care equipment.

ABBREVIATIONS USED

VRE	Vancomycin Resistant Enterococci
NNISS	National Nosocomial Infection Surveillance System
CDC	Centers for Disease Control
HICPAC	Hospital Infection Control Practices Advisory Committee
VRSA	Vancomycin resistant S. aureus
VRSE	Vancomycin resistant S. epidermidis
HCFA	Health Care Financing Administration

MICROBIOLOGY

Enterococci are relatively resistant to all classes of penicillins, as well as to cephalosporins, other beta-lactams, and aminoglycosides. High level amino-glycoside resistance and resistance to the glycopeptides vancomycin and teicoplanin have emerged rapidly as a result of selection, thus presenting a challenge for physicians who treat patients who have infections caused by these microorganisms. Treatment options are often limited to combining antimicrobials or experimental compounds that have unproven efficacy.

Enterococci are relatively hardy in the hospital environment. VRE have been cultured from a wide range of environmental objects studied during outbreaks, including the hands of health care workers, thermometers, bed rails and bed pans. Contact with hot water at 60 degrees centigrade for 1 minute does not kill the organism on bedpans.

The great concern surrounding VRE is the possibility of transmission of the vancomycin resistant plasmid to other gram-positive bacteria including other Enterococcus species, Streptococcus species, *Listeria monocytogenes*, or *Staphylococcus aureus*, resulting in a wide range of vancomycin and teicoplanin resistant organisms.

PREVENTION AND CONTROL

In September 1995 the Centers for Disease Control and Prevention (CDC) published the recommendations of the Hospital Infection Control Practices Advisory Committee (HICPAC) for the prevention and control of vancomycin resistance. Each hospital, through collaboration of its quality improvement and infection control programs, pharmacy and therapeutics committee, microbiology laboratory, clinical departments, and nursing, administrative and housekeeping services, is expected to develop a comprehensive, institution-specific, strategic plan to detect, prevent, and control infection and colonization with VRE. Such a plan will require coordinated, concerted efforts on the part of various hospital departments and must address all of the following elements:

- **Prudent vancomycin use**: Vancomycin use has been reported consistently as a risk factor for infection and colonization with VRE, and may increase the possibility of the emergence of vancomycin resistant S. *aureus* (VRSA) or vancomycin resistant S. *epidermidis* (VRSE). Therefore, all hospitals and other health care delivery services, even those at which VRE has never been detected, should develop a comprehensive, antimicrobial utilization plan to provide direction for their medical staff (including house-staff), oversee surgical prophylaxis practices, and develop guidelines for the proper use of vancomycin (Tables 1 and 2). A recent HCFA sponsored vancomycin utilization study in Rhode Island re-

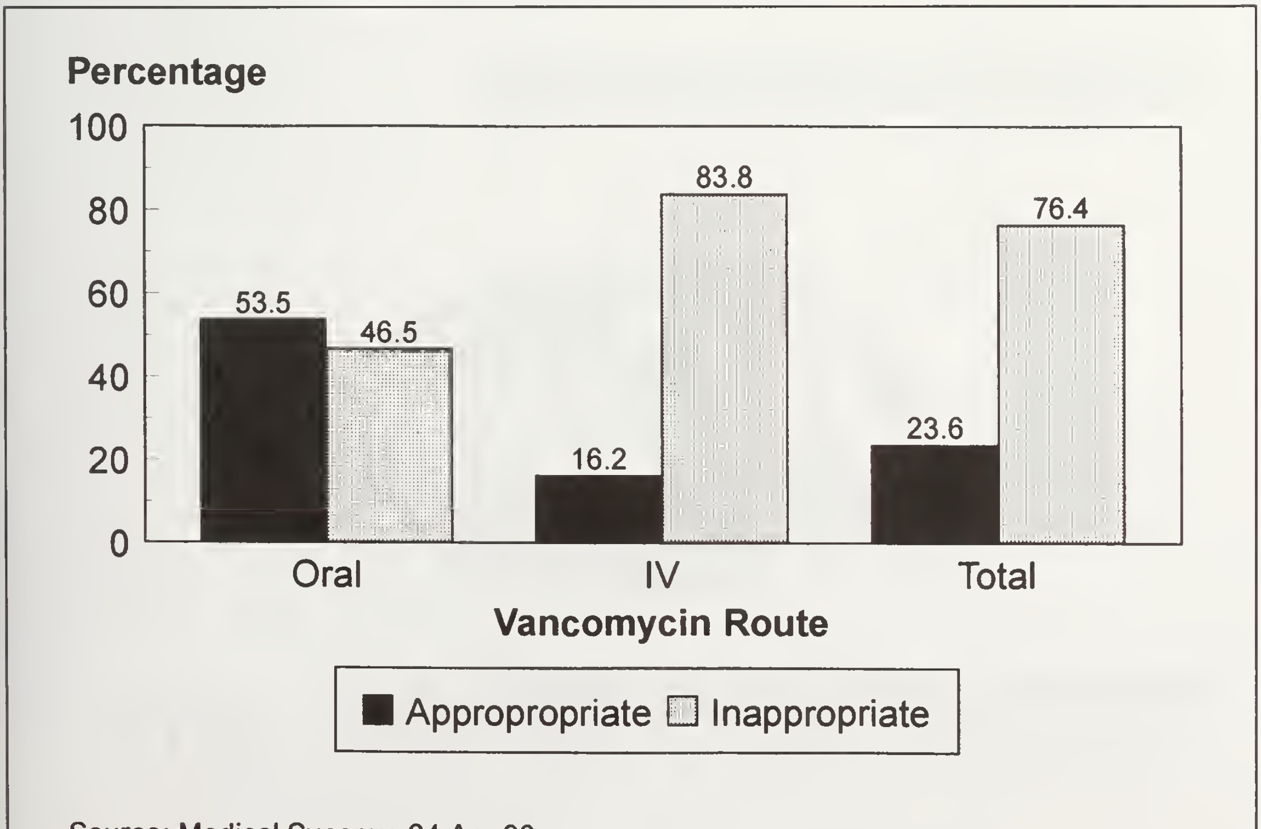
Table 1
Indications for vancomycin use

Intravenous:

- Treatment of serious gram-positive infections that are strongly suspected or proven to be resistant to all other antibiotic classes [If there is susceptibility to other agents, especially beta-lactams, they are preferred, being more rapidly bactericidal, less toxic and usually less expensive.]
- Treatment of serious gram-positive infections in patients with true beta-lactam allergy in whom no other antibiotic or beta-lactam is acceptable [Cephalosporins may be considered in patients who develop a rash after receiving penicillin. Allergy histories are frequently misleading or inaccurate, but careful questioning should ensure correct identification.]
- Prophylaxis for selected surgical procedures in patients who are at high risk of infection or endocarditis caused by resistant gram-positive organisms susceptible only to vancomycin [When so indicated, single dose prophylaxis is usually sufficient; rarely, a single additional dose may be necessary during a long operation.]

Oral:

- Life-threatening *Clostridium difficile* colitis
- Antibiotic-associated pseudomembranous colitis that has been unresponsive to oral metronidazole



Source: Medical Synergy, 24 Apr 96

Figure 1. Vancomycin utilization, severity level 1

vealed that the use of vancomycin at participating study hospitals deviated significantly from CDC guidelines, indicating that despite widespread dissemination of the guidelines, the inappropriate use of vancomycin is exceedingly common (Figure 1).

• **Education Programs:** Continuing education programs for hospital staff, including attending and consulting physicians, residents, pharmacy, nursing and laboratory personnel, and other direct patient-care providers should include information concerning the epidemiology of VRE and the potential impact of this pathogen on the cost and outcome of patient care. Because detection and containment of VRE require an aggressive approach and high performance standards for hospital personnel, educational sessions and innovative incentives to influence personnel behaviors may be indicated.

• **Role of the microbiology laboratory in the detection, reporting and control of VRE:** The microbiology laboratory's ability to detect VRE colonized/infected patients promptly and accurately is the first line of defense in implementing control measures in the health care setting. The microbiology

Table 2
Indications for vancomycin use

Intravenous:

- Routine surgical prophylaxis [Other antibiotics are more effective, cost less, and do not risk the development of VRE.]
- Empiric therapy for organisms expected to be sensitive to other organisms
- Treatment of organisms sensitive to other antibiotics expected to be efficacious
- Treatment of Methicillin resistant Staphylococcus epidermidis bacteremia or other clinical isolates in the absence of significant clinical infection [A thorough evaluation is necessary before instituting therapy; many of these isolates are contaminants rather than pathogens and are best managed without antibiotics.]
- Prolonged therapy, whether for prophylaxis, on an empiric basis, or for a proven infection, when there is neither active suspicion of nor positive cultures for MRSA or any other resistant gram-positive organism
- Eradication of MRSA colonization (eg, in sputum, nares or urine) [Not only is vancomycin frequently ineffective for this, it is potentially toxic.]

Oral:

- Selective decontamination of the digestive tract
- Empiric therapy for non-life-threatening C. difficile colitis
- Therapy for mild to moderate C difficile colitis that should respond to metronidazole

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laboratory also has the primary responsibility to detect and report the occurrence of VRSA or VRSE in the hospital.

- **Preventing and controlling nosocomial transmission of VRE:** Eradication of VRE is most likely to succeed when VRE infection or colonization is confined to a few patients on a single ward. After VRE has become endemic on a ward or has spread to multiple wards or to the community, eradication becomes difficult and costly. Aggressive infection control measures (isolation, cohorting, hand washing, barrier precautions, environmental hygiene and transfer policies) and strict compliance by hospital personnel are required to limit person-to-person nosocomial spread of VRE.

VRE In Rhode Island

As of April 1996, persons with VRE colonization and infection are required by regulation to be reported to the Department of Health. Several hospitals in Rhode Island have encountered and continue to deal with VRE colonization issues, as well as nosocomial transmission, discreet outbreaks, and low level endemicity. The Department of Health has recently developed guidelines for the control of VRE in nursing homes and extended care facilities. Copies are available by calling the Division of Disease Prevention and Control at 277-2577.

Though we live in an era in which there are many antibiotics, there are more resistant organisms to control than ever before. Only through aggressive education programs, targeting health care personnel behaviors, screening of patients at risk, strict enforcement of infection control measures, and judicious use of antimicrobials by physicians, can we prevent the chilling prospect of finding ourselves unarmed in the battle with the microbial world.

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Help Your Heart Recipes

This recipe is intended to be part of an overall healthful eating plan. Total fat intake should be less than 30 percent of your total calories for a day — not for each food or recipe.

Fresh Tomato Pizza

Vegetable oil spray
1 10-ounce package refrigerated pizza dough
3 or 4 medium Italian plum tomatoes, thinly sliced
¼ cup snipped fresh basil or parsley
Freshly ground black pepper
1 cup shredded part-skim mozzarella cheese

Preheat oven to 425° F.

Spray a 12-inch pizza pan with vegetable oil. Press dough evenly into prepared pan. Arrange tomato slices on top. Sprinkle with basil and season with pepper. Sprinkle with cheese. Bake 15 to 20 minutes or according to package directions. Cut into 8 wedges.

Serves 4; 2 pieces per serving. Preparation time: 10 minutes. Cooking time: 15 to 20 minutes.

Nutrient Analysis per Serving

284 kcal	Calories	**16 mg**	Cholesterol	**3 gm**	Saturated Fat
15 gm	Protein	**500 mg**	Sodium	**1 gm**	Polyunsaturated Fat
40 gm	Carbohydrate	**7 gm**	Total Fat	**2 gm**	Monounsaturated Fat

American Heart Association Quick & Easy Cookbook,
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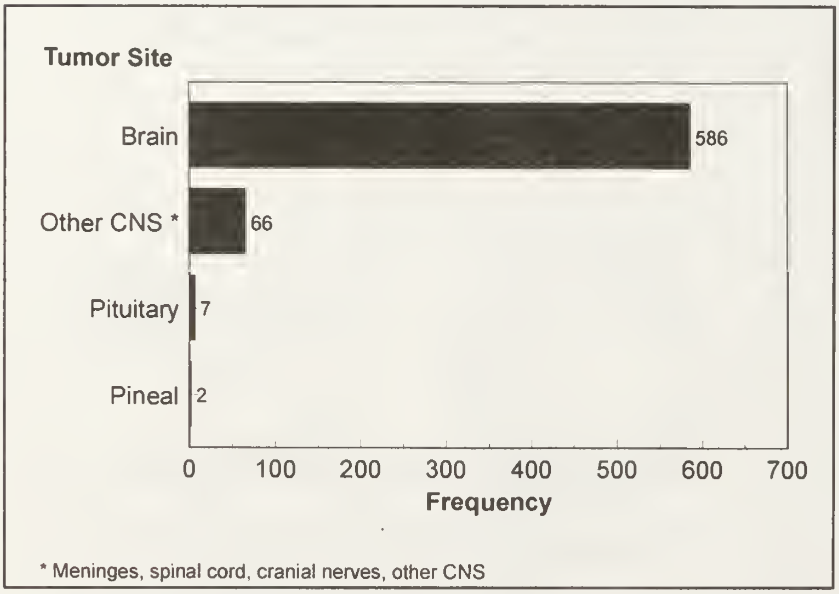
Health by Numbers

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Jay S. Buechner, PhD and William J. Waters, Jr., PhD

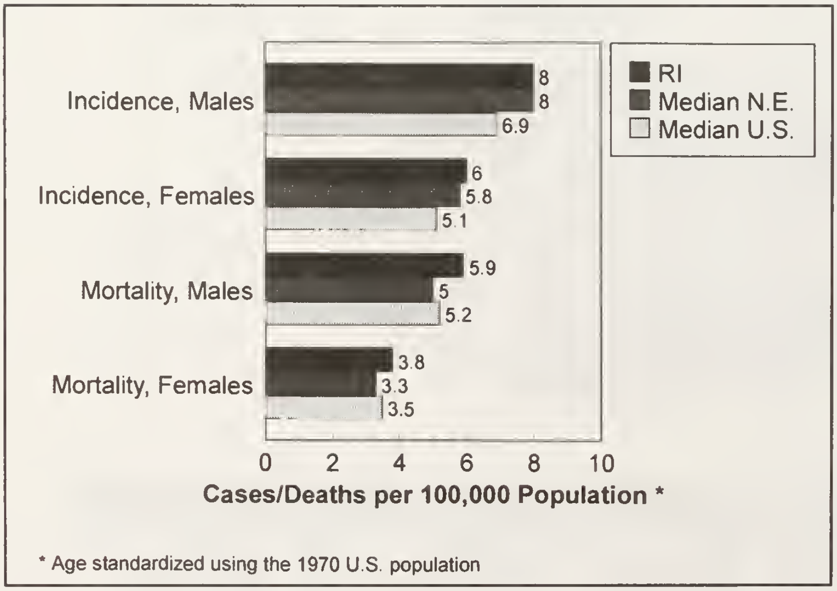
Tumors of the Brain and CNS in Rhode Island

John P. Fulton, PhD



* Meninges, spinal cord, cranial nerves, other CNS

Figure 1. Reported frequency of newly diagnosed malignant brain/CNS tumors among Rhode Island residents, 1987-1994, by tumor site.



* Age standardized using the 1970 U.S. population

Figure 2. Age-standardized brain/CNS cancer incidence and mortality, 1988-1991, Rhode Island, by gender, with median state values for New England and the United States.[1]

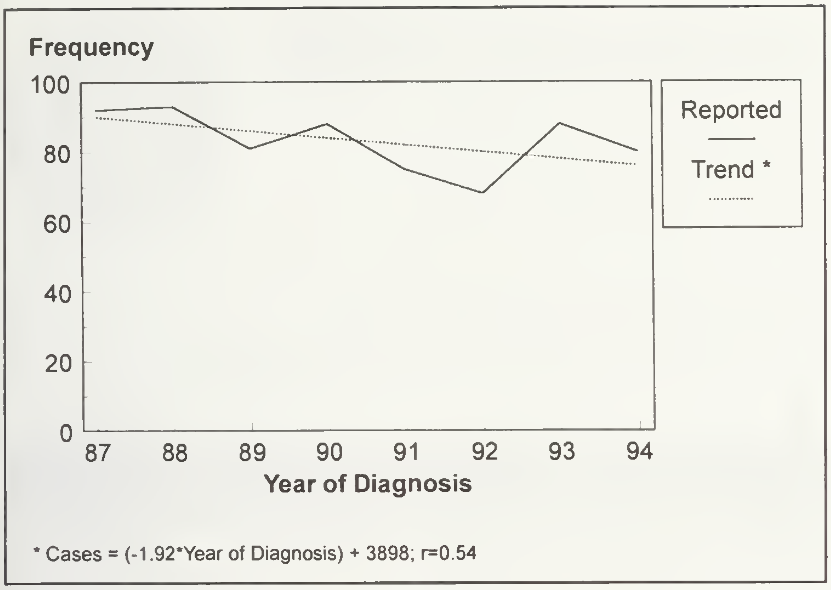
Dr. Fulton is assistant director, Division of Disease Prevention and Control, and clinical assistant professor of community health at Brown University.

OBJECTIVES

In order to assess whether to participate in the Central Brain Tumor Registry of the United States (CBTRUS), it is essential to know the incidence of benign and malignant tumors of the brain and central nervous system (CNS) in Rhode Island. For malignant tumors of these sites, the Rhode Island Department of Health (the Department) reviewed and summarized cancer registry data on tumors diagnosed among Rhode Island residents from 1987 through 1994. Although benign tumors are not currently reportable to the Department, they are of substantial concern because of their frequency, their case fatality rate, and their costs to society in terms of medical care and lost productivity. For these reasons registration of benign tumors is a requirement for participation of cancer registries in CBTRUS. The incidence of benign tumors of the brain and CNS for Rhode Island was estimated from data reported to CBTRUS.

METHODS

Distributions of malignant brain/CNS tumors by age at diagnosis, anatomical site, and histology were constructed from reports made to the Department on tumors diagnosed during the period 1987 - 1994 among Rhode Island residents. Codes for anatomical site were grouped into the following standard categories:[1] brain; meninges, spinal cord, cranial nerves, and other CNS ("other CNS"); pituitary; and pineal. Rhode Island resident deaths from malignant tumors of the



* Cases = (-1.92*Year of Diagnosis) + 3898; r=0.54

Figure 3. Reported frequency of newly diagnosed malignant brain/CNS tumors among Rhode Island residents, 1987-1994, by year of diagnosis, with regression line.

brain/CNS were identified from state vital records. Brain/CNS cancer incidence and mortality rates among Rhode Island residents were computed and age-standardized for comparison with CBTRUS data.[1]

The frequency of malignant brain/CNS tumors diagnosed among Rhode Island residents each year from 1987 through 1994 (adjusted for under-reporting from the Massachusetts Cancer Registry in 1994) was regressed on year of diagnosis to assess the trend in annual frequency of reported tumors.

The number of benign brain/CNS tumors diagnosed among Rhode Island residents, 1987-1994, was estimated using the average 1990-1995 malignant/benign tumor ratio for ten states participating in CBTRUS.[1]

RESULTS

An average of 83 malignant tumors of the brain/CNS were diagnosed annually among Rhode Island residents from 1987 through 1994. Among the 661 tumors reported to the statewide registry in that period, 586 (89%) occurred among adults (ages 20 and over, using the CBTRUS convention), and 75 (11%) occurred among children and teens (ages 0-19). About half (347, or 52%) occurred among males, and about half (314, or 48%) occurred among females. Almost all (644, or 97%) occurred among whites, eleven (2%) occurred among African Americans, and six (1%) occurred among people of other races.

The 586 malignant tumors of the brain represented 89 percent of the 661 reported brain/CNS tumors (Figure 1). 378 (57%) of the brain tumors occurred in the supratentorial region, 51 (8%) in the infratentorial region, 10 (2%) in the ventricles, and 147 (22%) in other regions of the brain. There were 66 (10%) malignant tumors of other CNS sites (meninges, spinal cord, cranial nerves, and other sites), seven malignant pituitary tumors and 2 malignant pineal tumors.

Among adults (ages 20 and over), astrocytomas and glioblastomas were the most common tumor histologies, accounting for 65% of the tumors reported from 1987 through 1994. Among children and teens (ages 0-19), astrocytomas and medulloblastomas were the most common tumor histologies, accounting for 57% of the tumors reported in the period of observation.

Age-standardized brain/CNS cancer incidence and mortality rates in for males and females Rhode Island during the period 1988 - 1991 were generally higher than the respective medians for New England states and for all states in the United States (Figure 2). (Incidence rates for this period are available for 30 states, including five of the six New England states, mortality rates for all 50 states.[1]) The one exception is the incidence rate for brain/CNS cancer incidence among males in Rhode Island, which is at the median New England value.

The annual frequency of malignant brain/CNS tumors among Rhode Island residents appears to be decreasing by about two cases per year according to the regression solution, although relatively large annual fluctuations occurred in the frequency of newly diagnosed cases from 1987 through 1994 (Figure 3).

The ratio of benign to malignant brain/CNS tumors reported to CBTRUS by ten member state registries for the period 1990-1995 is 0.63 to 1.00. If this ratio is applied to Rhode Island data for malignant tumors, an estimated 417 benign tumors were diagnosed in the State from 1987 through 1994, or an average of 52 cases per year. Judging from CBTRUS experience, many of these benign tumors would have been meningiomas.

DISCUSSION

Benign and malignant tumors of the brain/CNS represent a significant problem in Rhode Island, accounting for about 130 new cases and about 50 deaths per year. Recent brain/CNS cancer incidence and mortality rates for Rhode Island have generally exceeded state medians regionally and nationally. However, from 1987, the first full year for which Rhode Island incidence data are available, the frequency of malignant brain/CNS tumors in Rhode Island appears to have decreased. In the U.S. as a whole, brain/CNS cancer incidence increased among white males and females between 1973 and 1987, then levelled off.[1] If these trends continue, the Rhode Island incidence rates will approach the U.S. medians.

The Department is considering participation in CBTRUS, to support national surveillance and research on tumors of the brain and central nervous system. Central databases such as CBTRUS benefit participants by (1) providing comparative data to check

ABBREVIATIONS USED

CBTRUS	Central Brain Tumor Registry of the United States
CNS	Central nervous system

the accuracy and completeness of participants' data, (2) facilitating research by accumulating sufficient cases for effective statistical analysis, and (3) supporting the use of participants' data to investigate causes of disease and to develop policies and programs for the prevention and control of disease. Participation in CBTRUS would require the reporting of benign as well as malignant tumors of the brain/CNS, estimated to increase reporting by about 50 cases per year in Rhode Island. This issue will be discussed with providers, tumor registrars, and others throughout the state before a decision to participate in CBTRUS is made.

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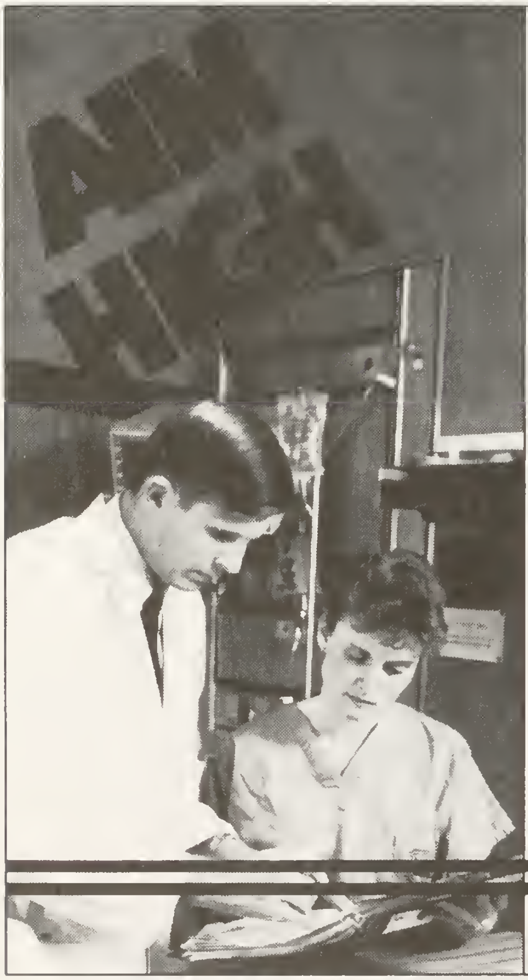

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AIR FORCE

Vital Statistics

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Roberta A. Chevoya

Rhode Island Monthly Vital Statistics Report
Provisional Occurrence Data from the Division of Vital Records

Vital Events

	Reporting Period		
	Dec. 1995	**12 months Ending with Dec. 1995**	
	Number	**Number**	**Rates**
Live Births	1,091	13,368	13.4*
Deaths	955	9,762	9.8*
Infant	(8)	(97)	7.3#
Neonatal	(4)	(75)	5.6#
Marriages	480	7,383	7.4*
Divorces	286	3,653	3.7*
Induced Terminations	455	5,706	426.8#
Spontaneous Fetal Deaths	82	977	73.1#
Under 20 weeks gestation	(79)	(913)	68.3#
20 + weeks gestation	(3)	(64)	4.8#

* Rates per 1,000 estimated population
# Rates per 1,000 live births

Underlying Cause of Death

	Reporting Period			
	June 1995	**12 Months Ending with June 1995**		
	Number (a)	**Number (a)**	**Rates (b)**	**YPLL (c)**
Diseases of the Heart	217	3,276	328.8	4,569.0
Malignant Neoplasms	200	2,438	244.7	7,141.0
Cerebrovascular Diseases	47	615	61.7	620.0
Injuries (Accident/Suicide/Homicide)	29	323	32.4	6,417.5
COPD	28	410	41.2	282.5

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.
(b) Rates per 100,000 current estimated population of 996,325.
(c) Years of Potential Life Lost (YPLL).

Note: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

THE RHODE ISLAND MEDICAL JOURNAL
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NINETY YEARS AGO

JUNE, 1906

The Journal summarizes the papers presented in a local symposium on the acute pneumonias of adults and children. Dr. W.L. Chapman first outlines the etiologic factors, the bacteriologic agents and the pathologic findings of the disease. Various precursor forces are mentioned including prior respiratory infection, external elements causing respiratory tract irritation, anesthetic agents, chest trauma and poor sanitation. In the great majority of cases the causative organism is the diplococcus, although microbial agents of syphilis and psittacosis must also be considered. The pathological findings are well-documented but one should be prepared to confront such complications as empyema, pericarditis, endocarditis, nephritis, otitis media and meningitis. Dr. Stephen A. Welch discusses the symptoms of the acute pneumonias, observing that in many instances the symptoms "may be so unmistakable that the physician can stand by the bedside and without physical examination tell which side is affected." At other times the symptoms may be so misleading as to suggest appendicitis. After a careful review of the major signs and symptoms and a description of the character and color of the sputum in various stages of pneumonitis, the author notes that increasing age tends to diminish the outward severity of symptoms. So too with the alcoholic, the pneumonia develops more insidiously. Dr. George S. Mathews discusses the diagnosis and prognosis of acute pneumonia concluding with: "It is well to keep hopeful in any case, no matter what the severity, for not infrequently the seemingly hopeless case may recover, through Nature's wonderful recuperative powers, aided by the judicious measures employed by the medical man." Lastly, the treatment of acute pneumonia is summarized by Dr. D.F. Gray. He acknowledges that no two physicians will treat pneumonia in a like manner, each using a variety of interventions including quinine, digitalis, serum, cold air, venesection, and creosotal. The author does advocate the following: purgatives [calomel and salines], nothing by mouth except fluids, alcohol baths if the temperature is high, and trional and codeine for restlessness. The author warns that cardiac stimulants [strychnia and whisky] be reserved for the inevitable crisis. Mention is also made, as a measure of desparation, of hypodermoclysis in those patients "who seem past every hope of recovery." He suggests hourly injections of 600 cc of hot saline in the flanks. Rectal injection may also be of benefit.

FIFTY YEARS AGO

JUNE, 1946

The Fifth Annual Chapin Oration, given by Joseph Stokes, Jr, MD is entitled *Recent Studies in the Prevention of Certain Infectious Diseases*. Stokes, Professor of Pediatrics at University of Pennsylvania School of Medicine, first discusses the nature and epidemiology of influenza, noting that there are two major strains, A and B. The pandemic strains, he states, are almost always strain A. He then relates the history of the development of an influenza vaccine using viral concentrations derived from chick embryo allantoic fluid. He presents field trials in U.S. Army personnel showing that the influenza vaccine is indeed effective. His studies also revealed that plasma pooling regularly yields substantial amounts of gamma globulin containing antibodies against numerous infectious diseases. In general, he observes, many epidemic diseases of childhood gradually immunize the general population both by apparent and inapparent cases. Examination of adult plasma, therefore, provides an index of epidemic trends. Gamma globulin from fractionated pools of plasma has been shown to give effective protection against certain viral diseases [eg measles] if given before exposure. Gamma globulin has not yet been shown to confer protection against poliomyelitis, however.

John F. Kenney, MD authors a paper entitled The Future of Medicine, representing his Presidential Address before the Rhode Island Medical Society. In the face of much speculation concerning governmental control of medical practice, he observes: ". . . the efforts of physicians would be replaced by politically-minded individuals whose principles will not be concerned with the best care of the patient, or continued study in medicine, but rather the desire to improve their position by currying favor of the political powers administering the medical and health programs."

The lead editorial expresses grave concerns over the progressive contamination and chemical pollution of the waters of Narragansett Bay.

TWENTY FIVE YEARS AGO

JUNE, 1971

In his Presidential address to the Rhode Island Medical Society, Richard P. Sexton, MD considers the impact on Rhode Island of a medical school at Brown University. He notes, first, that Rhode Island is a debtor state, sending fewer of its citizens to American medical schools than its estimated needs. Clearly, in his judgment, the state is in need of a local facility since out of state schools will necessarily favor applicants from their own state. The author then lists the reasons why Brown should be the site of a such an institution, building upon a preexisting six-year medical science program which has incorporated within it the first two years of formal medical education. The need for a State of Rhode Island financial commitment is stressed. Sexton concludes: "Such a program will need planning and discussion. It will primarily require community support, which will come from educating the populace to the need, the benefits, and the resultant improvement in medical manpower and medical care in this state."

Walter C. Bornemeier, MD, President of the American Medical Association discusses medical care for tomorrow, touching upon such critical elements as geographic maldistribution, the expansion of group practice, the growth of neighborhood clinics, changes in the nature of rural practice and, inevitably, partnership with government.

Thelma Ingles, RN writes on mobility in nursing and Bella Strauss, MD describes the Dartmouth program to train physicians' assistants [Medex.] Heber Youngken Jr., PhD, details those paramedical programs in Rhode Island designed to meet health care manpower needs in this region.

* * *

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Illustrations and charts must be submitted in black ink on white paper. Laser-printed graphs are acceptable, provided they are printed at 300 DPI resolution.

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Vol. 79 No. 7 July 1996

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COMMENTARIES

The Health of Rhode Island's MinorityPopulation

As a new director of the Rhode Island Department of Health, I asked the senior management of the Department to review our vision and mission and develop a strategic plan with me to reach that vision. We have articulated our vision: **All people in Rhode Island will have the opportunity to live a safe and healthy life in a safe and healthy community.** With this vision, it is immediately clear that we need strategies to improve the health and environment of those communities with the poorest health outcomes. Our experience and our data tell us that minority communities have the greatest disparities in health status. Minority communities are more likely to be poor and economically marginal, so illness and disability have a bigger impact on the well-being of families and communities, not just on individuals. Minority communities are more likely to encounter cultural and language barriers to obtaining prevention and treatment services and to participating in the political and social process.

When we begin to think seriously about how the Department of Health can work with minority communities to improve health status, our first thought is often about how we can change them into the "majority" community, like us. There is a significant body of research that indicates behavior change to promote distant outcomes, such as good health, is not so simple to achieve, even within the majority culture. Even our definitions of good health outcomes may not be the same.

Our strategic planning effort in decreasing the disparities in health status among Rhode Islanders is leading us in new directions, developing listening skills, promoting collaborative ventures, providing technical assistance, and broadening the sources of community input. This issue of *Medicine and Health/Rhode Island* is an open invitation to the medical community of the state to participate in the effort, improving the health status of minority communities and decreasing the disparities in health among Rhode Islanders.

Better understanding of our minority communities and their health needs comes in part from understanding the information base about those communities. It is also essential that we increase our listening skills collectively and invite minority communities into the dialogue about health. We hope this information helps you to participate in improving the health status of our minority communities.

Patricia A. Nolan, MD, MPH
Director of Health,
Rhode Island Department of Health

* * *

Making the Case for Minority Health

The word minority has become one of those words in the American political lingo that elicits very strong opinions regardless of the topic at hand. To some the word evokes memories of the Civil Rights struggle of the 1960's, to others it is synonymous with quotas and reverse discrimination. Regardless of where you stand in the political debate, when it comes to minority health it is difficult to ignore the reality that entire populations living in the most technologically advanced country in the world, have health standards that rival those of third world countries. It is also inescapable to conclude that it is in the best interest of the country to improve the health of all its inhabitants, given the fact that one way or another, the consequences of bad health outcomes in any group will impact the community as a whole.

Apart from the obvious need for social and economic justice as a moral imperative, there are real and measurable effects on the entire population when some of its members do not participate fully in the advancement of health standards. According to the Census Bureau between 1992 and 2005, it is estimated that 55% of net new workers entering labor markets will be minorities. The increased expenditures for the treatment of preventable diseases and the decrease in productivity that these diseases create threaten our economy and the entire fabric of this country. Each and every one of us should be compelled by this evidence to contribute to the elimination of these disparities. In response to this crisis, federal and state officials have introduced a number of initiatives some, of which are described in this issue of *Medicine and Health/Rhode Island*.

The purpose of the current edition is to present an overview of the health risks associated with minority status in our state. It is our hope that information on this critical topic will stimulate our readers to seek further information and knowledge on the issues presented. It is only with a solid knowledge base that an accurate diagnosis can be made and an effective treatment plan implemented that takes into account an individual's life circumstances.

Even though there is an increased likelihood of being impoverished if one is a minority, poverty alone cannot explain why health outcomes are different. There is a growing body of evidence that these differences cannot simply be explained by the traditional lifestyle risk factors such as smoking, exercise, and dietary patterns. Inadequate access to health care, while important, does not fully account for all disparities. Research conducted by Dr. Diane Rowley, Deputy Chief of Centers for Disease Control in Atlanta, found that African-American infants born to college- educated mothers had an 80% higher risk of dying in the first year than white babies born to college educated mothers, despite the fact that both groups had similar occupational stability, insurance, and access to health care. The implications for Public Health policy are great because simply providing ample safety nets for populations at risk may not bring the desired outcomes.

This brings us to the issue of discrimination and its impact on the health of minorities. The stress associated with belonging to a discriminated group and the environment that these groups are subjected to play a significant role in their health outcomes. In RI minority children are three times as likely to live in poverty as compared to white children. Nationally, minorities are more likely to live in counties that failed to meet EPA standards for air quality during the previous year. These are largely concentrated in urban areas of high unemployment, crime, nd substance abuse, the effects of which are just beginning to be investigated. The rapid spread of the AIDS epidemic among communities of color, as documented by Dr. Fisher in this issue, is evidence of health outcomes tied to socioeconomic and environmental variables. The compelling article by Miller and Webb, regarding violence as a public health issue, clearly demonstrates how living in an area where violence and firearms are commonplace puts everyone in that neighborhood at risk regardless of the individual's behavior.

For most practicing clinicians the political aspects surrounding the health of minorities are less important than their ability to deal with increasingly diverse patient populations Difficult clinical problems can become even more complicated by the clinician's lack of knowledge regarding the social and cultural circumstances which are essential in the understanding of any disease. When you add language barriers to this equation the diagnostic process becomes a virtual maze which puts the patient in peril and the physician at risk for medico-legal action. In this edition, Dr. Garcia-Colt's examination of cultural beliefs surrounding pregnancy illustrates quite well how someone's cultural background and experiences with racism can influence their perception of the health care system and how the system can fail when those personal beliefs are not understood and acknowledged. Also in this issue, Dr. Stanley Block writes on managed care and minorities sharing with us some of the pitfalls awaiting those trying to venture into this market. Suffice it to say that systems and policies aimed at suburban and well-to-do populations are not going to succeed in the "hood" (slang for neighborhood). Rules that require patients to call a Primary Care Provider prior to showing up in the emergency room, incorrectly assumes that one has a Primary Care Provider, not to mention a phone, some understanding of the medical situation at hand, and dominion over the English language.

Finally, though racism and discrimination are alive and well in America, it is ignorance, misunderstanding, and lack of communication between patients and providers that are the true enemy. Until we begin to recognize the monster in all of us and the Divine in all others, no amount of money or government initiative will be able to right the wrongs created by centuries of discrimination and inequality. It is the hope of the editors that this limited presentation, on what has become one of the most volatile issues of our time, will contribute to the fulfillment of Dr. Martin Luther King's dream. "That one day this nation will rise up to the true nature of its Creed. That all men are created equal."

Pablo Rodriguez, MD,Chair
Rhode Island Department of Health,
Minority Health Advisory Committee

Names, Names, Names . . .

During the past decade, this publication has chosen to simplify its name, first to *Rhode Island Medicine* [which explained its purpose with a minimum of words]; and now in January of 1996 - some six months ago - to *Medicine & Health/Rhode Island* [still economical with words but now reflecting its broadening educational and public health mission.]

The Editorial Board, of course, had numerous traditional names from which to choose, many honored by historic linkage with great medical publications. But had the meanings of many of these names been earnestly explored and believed, we would surely have portrayed our state publication inaccurately.

Take, for example, the most widely used name for a medical publication: *Journal*. The name stems circuitously from the Latin, *diurnis*, meaning daily, which if used would be a patent deception since we are inflexibly a monthly publication. *Annals*, from the Latin *annus*, meaning a year, suggests that we appear in print but once every 12 months, again an inaccurate description. *Chronicle* [from the Greek, *chronos*, pertaining to time] should be reserved for those publications, such as diaries and church records which are heavily time-oriented. *Archives* is derived from the Greek *archeia*, meaning ancient or principal place and describes a public building to maintain documents - or the documents themselves. *Bulletin* comes from the Latin, *bulla*, a seal upon a document [or medically, a blister.] Its meaning evolved into a term describing a papal edict, a Bull. The Italian diminutive became *bulletina*, and in English, bulletin.

The word *gazette* [as in *Boston Medical and Surgical Gazette*] has an interesting history. The Latin, *gaza*, meaning treasure in the abstract, is derived from the Hebrew word *genizah* which defines a synagogue storeroom for treasured texts.. A small coin of renaissance Venice bore the name *gazetta*, the Italian diminutive of *gaza*. It was the cost charged for a copy of the monthly Venetian newspaper and the name of the coin was eventually transferred to the name of the publication, which in English becomes gazette. [Magpies are known to collect shiny pieces of glass and metal; and for this reason are also called *gazettas*.]

A widely distributed 12th century secular poem described the whoremonger, Pamphilus [from Greek *pan-*, all; and *philus*, love]. The tract was immensely popular, going through innumerable copyings. With the advent of printing some 300 years later, the ode received an even wider distribution. The subject of the tract, Pamphilus, became the generic name for all small, cheap and impermanent publications, something now called pamphlets.

The word, *magazine*, is an uncommon name for a medical publication. It derives from the Italian, *magazzino*, which in turn is taken from the Arabic word *khazana* meaning storehouse, an earlier meaning still preserved in phrases such as munitions magazine.

Two names merit special recognition: *Transactions* and *Proceedings*. On the 28th of November, 1660, a group of English scientists convened in London to hear a paper presented by Mr. Christopher Wren. The meeting represented the first formal gathering of a group intent on *"founding a Colledge for the promoting of Physico-Mathematicall Experiementall Learning."* By 1661 this group, now meeting on a regular basis, earned the endorsement of King Charles II as the Royal Society. The Secretary of the Society, Henry Oldenburg, maintained an active correspondence with scientists and thinkers throughout Europe. These letters, sharing new scientific observations, forming the nucleus of the Society's first periodical, *Philosophical Transactions*, a publication which continues, without interruption, to this day and is regarded by most historians as the oldest scientific periodical in the world. In 1832 the Society developed yet another publication which incorporated abstracts of physical, mathematical and biological papers and was called *Proceedings of the Royal Society*. The title, *Transactions* , was probably chosen to define its purpose: to describe the current activities of the authors [Latin, *transactus*, to carry through.] *Proceedings* [Latin, *procedere*, to go forth, to advance] was meant to establish an enduring record of the authors' advances in the physical and biological sciences.

There are still other names frequently used for medical periodicals: Review [Latin, *re* and *videre*, to see again]; Advances [Latin, *ab ante*, meaning from before]; Record [Latin, *recordari*, to rethink, to remember; at a deeper level, to remember in the heart as in *cordis*]; and Digest [Latin, *digestus*, to carry apart, to distribute], but these names no longer carry their former specificity.

Given the splendid list from which to choose when determining the name of its publication - and the intimidating historic weight that some of these names carry - this Editorial Board elected finally to lean toward brevity rather than elegance.

Stanley M. Aronson, MD

Acknowledgement . . .

The Co-Editors of this issue wish to acknowledge the many contributions of Pheamo Witcher, Minority Health Coordinator at the Rhode Island Department of Health. Ms. Witcher was very instrumental in the planning, organization, coordination, and writing of this work. Without her dedication and tireless efforts, this issue would not have been possible.

We would also like to acknowledge the contributions of Ms. Diane Collins who typed many of the manuscripts.

Differences in Health Status among Racial and Ethnic Groups in Rhode Island

Jay S. Buechner, PhD

The national public health agenda for this decade was established with the publication in 1990 of *Healthy People 2000: National Health Promotion and Disease Prevention Objectives* for the Nation[1] by the United States Department of Health and Human Services. This document established targets for the nation in twenty-two broad areas, stemming from three overall goals:

1) Increase the span of healthy life for all Americans;

2) Reduce health disparities among Americans; and

3) Achieve access to preventive services for all Americans.

The adoption of the second of these three goals recognizes the fact that the health status of certain sub-groups within the nation's population, including groups defined on the basis of income, age, disability, and race and ethnicity, falls consistently below that of the majority of Americans. Thus, while establishing 300 health objectives for the nation's entire population, *Healthy People 2000* also included 223 sub-objectives for special populations. Over half (114) of these sub-objectives addressed the health status of special populations defined by race and ethnicity.

Objective 22.1 in the Priority Area for Surveillance and Data Systems directed "the development of a set of health status indicators appropriate for Federal, State, and local health agencies...". In response, the Centers for Disease Control and Prevention, through the Committee 22.1, a group of public health professionals, selected 18 measures covering health status and individual risk for disease or premature death.[2] These 18 measures were established as the Health Status Indicators that are to be used to present a summary evaluation of the health condition of a defined population, be it a population residing in a specific geographic area or a population sharing a common characteristic. In this analysis, the Healthy People 2000 Health Status Indicators are presented for groups within the Rhode Island population defined by race and ethnicity, in order to characterize the differentials in health status among these groups.

ABBREVIATION USED

AIDS	*Acquired immune deficiency syndrome*

METHODOLOGY

Details of the methodology used to compute the Health Status Indicators for racial and ethnic groups in Rhode Island have been published previously.[3] Of the thirteen indicators presented and discussed here, six are age-adjusted mortality rates computed from the death certificate file of the state's vital records, three are crude incidence rates computed from reportable disease files for the state, three are rates of risk factors relating to maternal and child health computed from the birth certificate file of the state's vital records, and the infant mortality rate is computed using both the birth certificate and death certificate files. Where necessary, multiple years of data from these sources have been combined to assure that rates are based on meaningful numbers of cases. Population counts used for rates are from the 1990 United States Census for Rhode Island. Age-adjusted rates are standardized to the 1940 United States population in order to retain comparability with national data as defined in **Healthy People 2000**.[1]

Data for five of the Health Status Indicators are not presented here. In three cases data by race and ethnicity were not available for the indicator as specified (mortality rate for work-related injuries, proportion of children under 15 years of age living in families at or below the poverty level, and proportion of persons living in counties exceeding U.S. Environmental Protection Agency standards for air quality during the previous year). In one case (suicide rate) the most recent data were not consistent with patterns from pre-

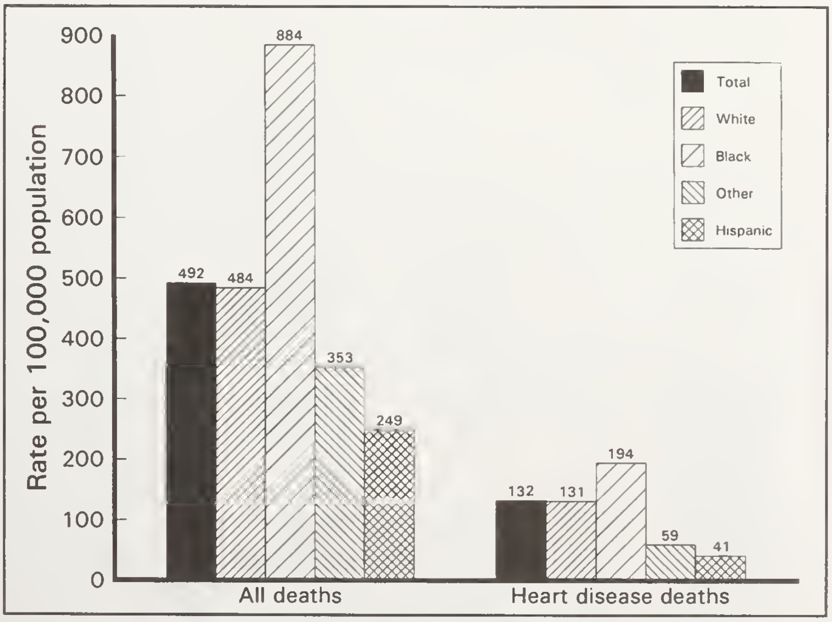

Figure 1. Age-adjusted death rates for all causes and for diseases of the heart, by race and Hispanic origin, Rhode Island, 1989-1991.

vious years, and it could not be determined whether the observed change represented a change in trend or a one-time fluctuation. In the final case (incidence of measles) the number of reported cases over the four-year period was inadequate for comparing rates in sub-populations with confidence.

Wherever possible, data have been computed for the following four groups: White, non-Hispanic ("White"); African-American ("Black"); White, Hispanic, and Hispanic persons of "other" races ("Hispanic"); and Native American, Asian and Pacific Islander, and non-Hispanic persons of "other" races ("Other"). Deviations from these standard categories include the following: (1) for infant mortality and for the three risk factors relating to maternal and child health, "Hispanic" includes Hispanic persons of all races; (2) for tuberculosis rates, cases with "unknown" race and ethnicity are included in the "White" group.

> *Members of the Black community in Rhode Island experience higher rates than their White counterparts in all thirteen measures of mortality, disease incidence, and risk factors.*

RESULTS

Data from the 1990 Census for Rhode Island by race and ethnicity are presented in Table 1.[4] For the standard groups used in this analysis, 1990 Census populations are as follows: White - 896,109 (89.3%); Black - 38,861 (3.9%); Hispanic - 39,991 (4%); Other - 28,503 (2.8 %). A detailed description of Rhode Island's population by race and ethnicity has been published previously.[5] Notable population increases between 1980 and 1990 occurred among persons of Hispanic ethnicity (132%) and among Asians and Pacific Islanders (246%). The rapid growth in these two groups is thought to have occurred primarily through immigration from their native countries, so that many individuals in these groups are likely to face difficulties such as language barriers and cultural differences that impact on their health status.

Table 1
Population by Race and Ethnicity (Hispanic Origin), Rhode Island, 1990

Ethnicity/Race	Population Number	Population Percent*
Hispanic Origin		
White	21,266	2.1
Black	4,578	0.5
American Indian, Eskimo, or Aleut	442	0.0
Asian or Pacific Islander	741	0.1
Other Race	18,725	1.9
Subtotal	45,752	4.6
Not of Hispanic Origin		
White	896,109	89.3
Black	34,283	3.4
American Indian, Eskimo, or Aleut	3,629	0.4
Asian or Pacific Islander	17,584	1.8
Other Race	6,107	0.6
Subtotal	957,712	95.4
Total	1,003,464	100.0

*An entry of 0.0 indicates a percentage of <0.05.

Age-adjusted rates for all of the mortality Health Status Indicators show wide disparities by race and ethnicity in Rhode Island. For deaths from all causes and deaths from the leading cause, heart disease, the rates for the Black population greatly exceeded the rates for the White population, while the rates for the Hispanic and Other groups fell below the White rate and the state rate overall. (Figure 1) For all-cause mortality in particular, the Black rate showed an excess of 83% over the rate for White residents.

Similar patterns were seen for mortality from lung cancer and breast cancer, for which Black mortality rates exceeded all others. (Figure 2) At the other extreme, mortality rates for these causes among Hispanics were much lower than those for other groups, especially for lung cancer. Rates for those in the Other race/ethnicity group were below the White rates for both causes.

For the two remaining mortality Health Status Indicators, different patterns emerged. (Figure 2) Rates of death caused by motor vehicle crashes showed little variation among the race and ethnic groups examined, except for a much lower rate among the Other group than among White, Black, and Hispanic residents. On the other hand, the rate of death from homicide showed the largest relative variations of any mortality Health Status Indicator investigated, with nearly a nine-fold variation among groups. The homicide rates for Hispanic residents and residents of Other race/ethnicity were also highly elevated relative to the White rate.

Infant mortality is one of the Health Status Indicators relevant to maternal and child health. Though declining in all populations in recent years, the infant mortality rate remains higher in the Black population than in all other subpopulations based on race and ethnicity, and by a considerable margin. (Figure 3) This excess is mirrored by the high prevalence of risk factors for poor infant health among Blacks, including high rates of low birthweight babies, of late entry to prenatal care, and of adolescent mothers. (Figure 4) Hispanic newborns and newborns of Other races also showed higher than average prevalence of these same risk factors, but relatively low infant mortality rates.

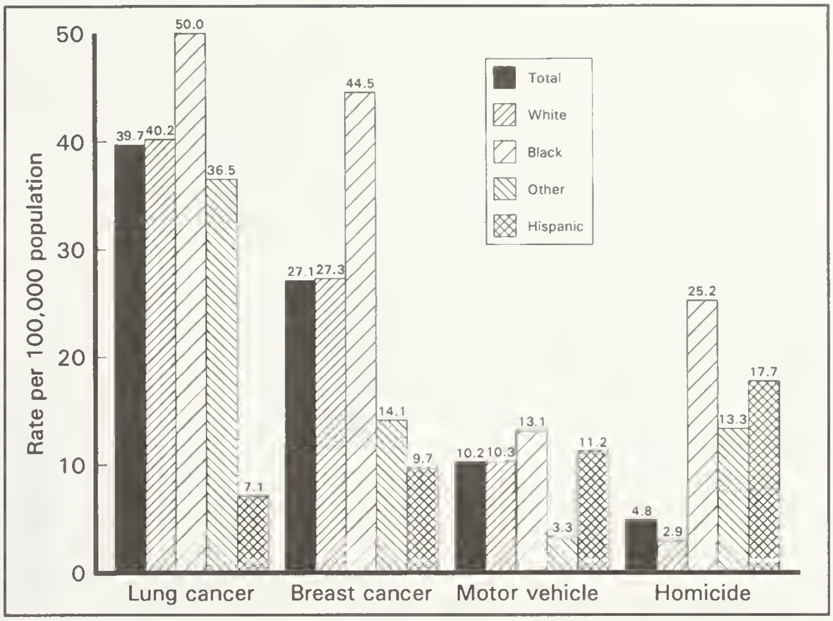

Figure 2. Age-adjusted death rates for selected causes, by race and Hispanic origin, Rhode Island, 1989-1991.

Incidence rates for the reportable diseases included in the Health Status Indicators again show large variations among different racial and ethnic groups. (Figure 5) The variation is most evident in the rates for AIDS incidence, for which the Black rate is over eight times the White rate and for incidence of syphilis, for which the Black rate is over 25 times the White rate. The rates of incidence for these diseases among Hispanics are also elevated relative to the White rates, but not to the same extent. The pattern for incidence rates for tuberculosis differs from those for AIDS and syphilis in that the highest observed rate is for persons of Other races, but the incidence rates for Blacks and Hispanics are higher than the White rate for this indicator, too.

Overall, members of the Black population in Rhode Island experience higher rates than their White counterparts in all thirteen measures of mortality, disease incidence, and risk factors. For eleven of the measures, their rates were the highest among all groups included. Hispanic residents experience excesses in eight of the thirteen measures, with their high rates concentrated in the disease incidence indicators and the risk factor indicators, rather than the mortality indicators. For residents of Other races, only in five of the thirteen measures do their rates exceed those for Whites, and three of those are the measures of risk for poor birth outcomes.

Discussion

As measured by these indicators, the health status of the Black population in Rhode Island, and to a lesser extent, that of the Hispanic population, suffers in comparison with the health status of the White population. For those of Other races, the health status indicators are more typical of the population as a whole. However, there may be sub-groups within that heterogeneous category whose disadvantage in health status is obscured by inclusion with healthier sub-groups. Overall, the variation in these indicators confirms that disparities in health within the state's population persist and that these disparities need focused attention if they are to be reduced or eliminated.

It has also been observed in this analysis that improvements are needed in the ability to identify and track disparities among sub-populations defined by race and ethnicity in Rhode Island.[6] The need for improved measurement capabilities where the indicators can not be specified by race and ethnicity is clear, as is the need for measurement of health status in smaller groups within

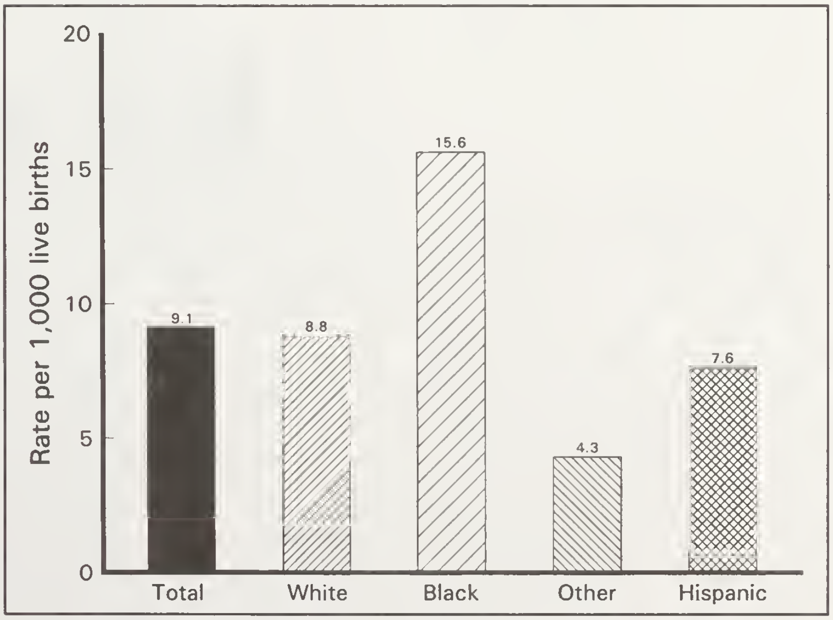

Figure 3. Infant mortality rate, by race and Hispanic origin, Rhode Island, 1989-1991.

the categories used here. It is also a concern that studies at the national level have determined that mortality among racial and ethnic groups other than Whites and Blacks has been substantially underestimated in the current vital records system.[7] These issues are among those that are being investigated in Rhode Island in an effort to improve the ability of the data system to support planning and interventions that will work to reduce health disparities such as those presented here.

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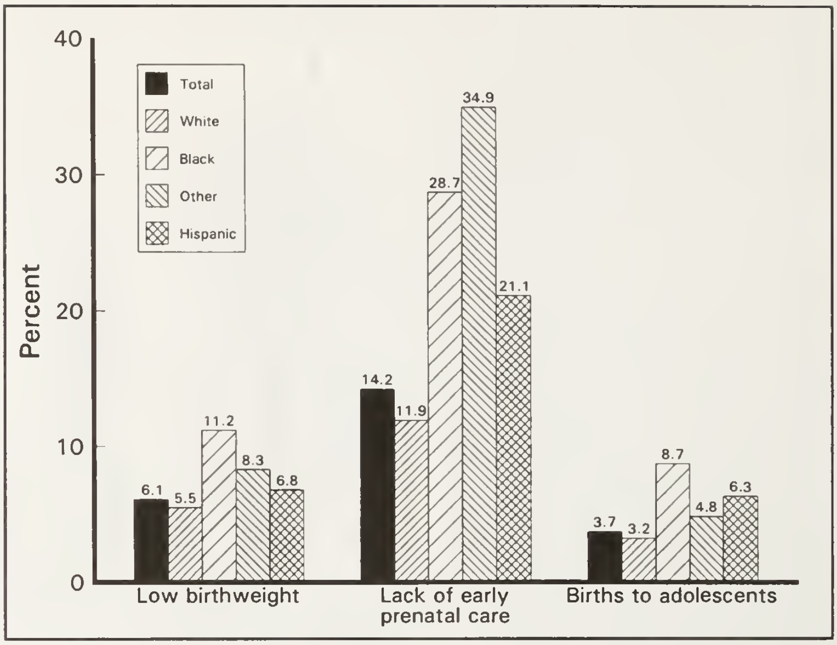

Figure 4. Maternal and infant health risk factors, by race and Hispanic origin, Rhode Island, 1989-1991.

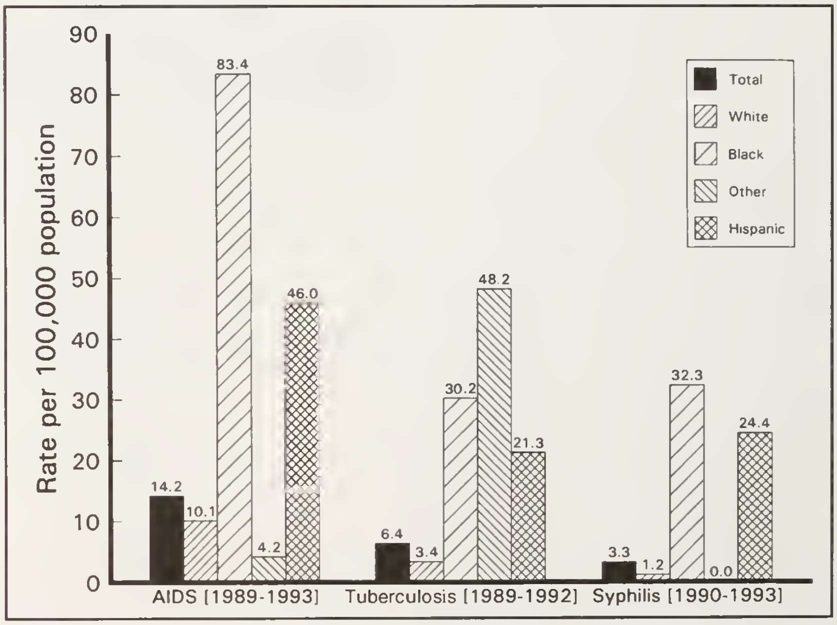

Figure 5. Incidence rates for selected diseases, by race and Hispanic origin, Rhode Island.

The Rhode Island Department of Health Minority Health Program

Pheamo R. Witcher, MCP

"Despite the unprecedented explosion in scientific knowledge and the phenomenal capacity of medicine to diagnose, treat, and cure disease, African-Americans, Hispanics, Native Americans and those of Asian/Pacific Islander heritage have not benefited fully or equitably from the fruits of science or from those systems responsible for translating and using health sciences technology". (U.S. Department of Health and Human Services. Report of the Secretary's Task Force on Black and Minority Health. Washington, D.C., August 1985).

INTRODUCTION

Racial and ethnic minority populations throughout the U.S. suffer disproportionately from poor health outcomes and premature mortality. Compared to the non-Hispanic White population, minority populations experience higher rates of infant mortality, a higher incidence rate of infectious diseases, higher rates of injury and homicide, and a higher incidence of most chronic diseases such as heart disease, cancer and diabetes. The causes of poor health among minority populations are varied and include inadequate access to preventive health care and barriers to health care such as, but not limited to, lack of health insurance and lack of culturally and linguistically appropriate care. Lifestyle factors such as smoking, alcohol consumption, inadequate diet, and lack of exercise also contribute to less than satisfactory health outcomes.

ABBREVIATIONS USED

AIDS	Acquired immune deficiency syndrome
HIV	Human immunodeficiency virus
MHP	Minority Health Program
OMH	Office of Minority Health
OMHRC	Office of Minority Health Resource Center
RIDH	Rhode Island Department of Health

NATIONAL RESPONSE

These disparities in health status were documented in the 1985 landmark report, *Report of the Secretary's Task Force on Black and Minority Health*. The findings in this report led to the creation of a National Office of Minority Health (OMH) as well as a nationwide network of State Offices of Minority Health. Currently, there are thirty-two such entities. The mission of OMH is to improve the health of racial and ethnic minority populations through the development of health policies and programs.

To attain its mission, OMH serves as a focal point for consultation, technical assistance, collaboration, and coordination of efforts within the U.S. Department of Health and Human Services on strategies, policies, and programs to improve minority health. OMH concentrates its efforts on the health problems which have led to excess mortality and morbidity rates among minority populations: alcohol and other drug use, cardiovascular disease and stroke, cancer, diabetes, infant mortality, violence and HIV/AIDS. OMH also addresses "cross cutting issues" essential to improving the health of minority populations. These issues include: access to health care, cultural competency in health service delivery, improved health data, and the availability of health professionals to serve minority populations.

One of OMH's most notable achievements is the establishment of the Office of Minority Health Resource Center (OMHRC). The Resource Center facilitates the exchange of information regarding the health status of racial and ethnic minority populations nationwide through the provision of a number of free services to health care professionals, community based organizations, and others. These services include the publication of a minority health newsletter, mailing lists, database searches, and expert referrals.

RHODE ISLAND RESPONSE

In 1987, the Rhode Island Department of Health (RIDH) initiated a number of activities aimed at reducing health disparities between the state's minority and Non-Hispanic White populations. These activities included initiation of improved methods for the assessment and tracking of minority health, improving dialogue between representatives of the minority community and the RIDH, and establishing minority task forces on AIDS and on minority male health. Further, several federally funded minority health programs were launched and two major minority male health conferences were convened.

MINORITY HEALTH PROGRAM

In 1992, the State of Rhode Island enacted the Minority Health Promotion Act in an effort to develop a long-term, on-going and organized commitment to improving the health status of minority populations in Rhode Island. The Act called for the establishment of a minority population health promotion program to provide health information, education, and risk reduction activities to reduce the risk of premature death from preventable diseases in minority populations. Subsequently, the Minority Health Program was established within the Rhode Island Department of Health.

Since its inception, the Minority Health Program (MHP) has employed four mechanisms for improving the health status of Rhode Island's minority populations. These include: establishing and maintaining partnerships with minority populations to ensure their involvement in programs and policies developed to address these discrepancies; providing funding for the development of minority health promotion programs; provision of capacity building and technical assistance to minority populations; and promotion of internal coordination amongst all

RIDH programs and initiatives which provide services and support to minority populations.

Partnerships with Minority Populations

Through the provision of staff support to the Director's Minority Health Advisory Committee, the MHP works closely with representatives of the minority community. This multi-racial/multi-ethnic committee is composed of representatives from all the major racial and ethnic groups within the State of Rhode Island, including persons of African-American, Hispanic, Asian and Pacific Islander and Native American descent. This group is charged with advising the Director of Health on health issues of concern to the minority community. Since its inception four years ago, The Minority Health Advisory Committee has been instrumental in a number of activities, including shaping the development and the ongoing activities of the MHP; establishing the minority health promotion grant program; and providing on-going guidance and advice to the Department in the areas of programs, planning, surveillance, and outreach efforts which target minority populations.

Funding Community Based Agencies

The Minority Health Promotion Grant Program administered by the MHP has awarded nearly $850,000 in grants to not-for-profit community based agencies serving minority populations. The grants are awarded through a request-for-proposal process by the Minority Health Advisory Committee, which also chooses the priority areas for funding. For Fiscal Years 1994-1996, three priority areas have been recommended for funding: reducing violent and abusive behavior; reducing the number of women under the age of 18 who become pregnant; and increasing access to primary care for minority populations. For fiscal year 1997, the Minority Health Advisory Committee chose just one priority area for funding – enhancing access to primary care. A total of 36 grants have been awarded to 21 non-profit community based agencies since the beginning of the grant program.

Capacity Building and Technical Assistance

Capacity building and technical assistance programs offered by the MHP since 1993 include a medical interpreters program and a grant writing workshop for minority community-based agencies serving minority populations. Each of these are described below:

Medical Interpreters Program

Using a $15,000 mini-grant from the Association of State and Territorial Health Officials in 1993, the MHP hired a consultant to train 25 medical interpreters employed at health care clinics, hospitals, and the Department of Health. Coursework included information on the role of the interpreter, translations of medical terminology, discussions of various methods of interpreting, and more specific information regarding pediatrics, mental health, death and dying. Monies from the grant were also used to train health professionals on how to work more effectively with medical interpreters.

> *Health disparities in Rhode Island have not appeared overnight; nor will they disappear quickly or easily.*

Grant Writing Workshop

In September of 1995, the MHP offered a grant writing workshop for community-based agencies serving minority populations. The rationale for offering this workshop was to enhance the ability of minority community-based agencies to identify, access and obtain funding on a local, state and national level for the purpose of developing minority health promotion programs. The MHP is currently working in conjunction with the Minority Health Advisory Committee to develop additional capacity building workshops for minority community based agencies, focusing on such topics as fundraising, board and organizational development.

Internal Coordination

In October of 1995, the MHP convened the Internal Minority Health Coordinating Committee. The purpose of this committee is to improve coordination and collaboration among all Department of Health programs on minority health issues. Through this committee, the MHP serves as a focal point for consultation, technical assistance, collaboration, and coordination of efforts within the RIDH on strategies, policies, and programs to improve minority health.

The Challenge Ahead

Health disparities in Rhode Island have not appeared overnight; nor will they disappear quickly or easily. The Department of Health, health care professionals and minority community leaders must work together to develop a proactive agenda for change which will result in improved health outcomes. Further, in order for this agenda to succeed, it must embrace the diversity that exists within Rhode Island's racial and ethnic minority populations.

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Cultural Differences in Beliefs and Practices about Pregnancy and Childbearing

Cynthia Garcia Coll, PhD and Katherine Magnuson

Cultural beliefs and practices surrounding pregnancy and childbirth are an important point of consideration for medical professionals practicing in our country and especially in Rhode Island. It has been estimated that approximately 600,000 legal newcomers, mostly Asian and Latin Americans, arrive yearly in the United States. When estimates of illegal aliens are also counted, the number of newcomers rises to a million or higher.[1] The 1990 census reported 19.8 million foreign-born persons in the United States and 95,088 foreign-born persons in Rhode Island, close to 10% of the state's population.[23]

The importance of considering different populations' cultural beliefs about pregnancy and childbirth is substantiated by a variety of facts. First, many immigrant populations have high fertility rates. Rumbaut and Weeks found that Indochinese women had per average 5.6 children, whereas American women only averaged 1.8 children.[4] In addition, many immigrant populations are also relatively younger than American-born populations.

Furthermore, many immigrant and minority populations are considered high-risk for child birth outcomes. Some populations of minority women suffer an excess risk of contracting sexually transmitted diseases, have higher rates of maternal and infant mortality, lower rates of prenatal care, and a higher incidence of teenage pregnancy.[6] Ironically, although minority women can be considered a high risk population, research shows that some recent immigrants have better pregnancy outcomes than native born African-American, Non-Hispanic white Americans, and second and third generation immigrant women.[7-8] Various lines of research have found that "Americanization" can be manifested in low family support for pregnancy, higher use of alcohol, cigarettes, or drugs, and an emphasis on fast food. The adoption of these lifestyles by acculturating women has a negative impact on childbirth outcomes, and thus second and third generation immigrant pregnant women have poorer pregnancy outcomes compared to more recent immigrants.

The large numbers of foreign-born women living in the United States, these populations' high fertility rates, relatively younger ages, high risk status, low risk paradox, and under utilization and differential patterns of utilization of health care systems all underscore the importance of considering cultural beliefs and practices surrounding pregnancy and childbirth.

THE ROLE OF CULTURAL BELIEFS AND PRACTICES IN HEALTH CARE

Many newcomers to the United States "have a foot in two cultures."[1,12] Although middle class immigrants might share their doctors' belief systems in scientific medicine, many of the poorer immigrants do not. Consequently, when health care providers are serving populations which do not share either an understanding nor a belief in our medical system, issues arise which might compromise the quality of care that is delivered. However, having a knowledge of and respect for the preferences and taboos of immigrants' and other cultural groups' more traditional medical systems, can allow medical professionals to be both more effective and more efficient.[1]

The cultural differences between North Americans' and immigrants' or minority populations' understandings of health care issues can have serious health consequence during pregnancy and delivery. These populations can have different conceptualizations about illness and health that directly affect their interactions with our medical care system. Individuals in cultures which do not accept mental illnesses or psychological stress, particularly Latino and Asian cultures, frequently manifest their psychological distress in physical symptoms, blurring the distinction between mental and physical health.[13] Furthermore, different cultures may believe that physical illnesses are caused by supernatural or spiritual forces such as a curse or a punishment for bad behavior.[13] For example, the Hmong believe that their body contains a number of souls, some of which are attached to particular organs, and that an illness is the result of the loss of a soul which can occur when an individual is sleeping or has been frightened.[14] Several Latino and Asian cultures also have a system of beliefs that classifies illnesses and physical conditions as either hot or cold and attributes them to an imbalance of the body's natural hot/cold equilibrium, or as it is termed in many Asian cultures the yin/yang equilibrium.[13, 15]

A culture's etiologic understanding of illness and health has very concrete implications for a course of treatment. Many different cultural groups have a folk tradition of medicine base on their particular understanding of sickness, and thus use a variety of non-medical home remedies and cures, rather than seeking standard medical care. Often members of cultural communities rely on these folk remedies first, to remove the cause of the disease, and then only seek biomedical treatment to relieve the physical symptoms of the disease. It is thus important for health care professionals to remember that adherence to biomedical treatment plans does not and should not preclude the discontinuation of harmless alternative remedies or home cures. These populations often consider themselves sick unless they have followed a folk treatment that they believe will remove the cause of the illness.[16]

In addition, when an individual does seek bio-medical health care and the prescribed treatment does not meet her expectations, she might not adhere to the prescribed treatment. Thus, a woman who has a condition classified as "hot," might not take vitamins because they too are classified in her traditional belief system as "hot," and thus they are believed to exacerbate the hot condition rather than restoring the hot/cold equilibrium.[16]

However, the woman might be more willing to take the vitamins if she is instructed to do so with a beverage that is classified as cool.[16] Furthermore, it has been found that when prescribed treatments do not match patients' expectations they will seek care from several different providers. Scott described how a woman was not satisfied with treatments prescribed for her child's cold until the child was administered a shot, because she believed that only an injection could cure her child.[16]

Members of different cultures might have a different process of making health care decisions than most Americans. These decisions for different cultural groups varies both in terms of who is included in the decision making process and how a decision is reached. For example, the decision making process for Mexican-Americans and the Hmong might include the entire extended kinship system reaching a consensus.[14, 17] In contrast, Hoang and Erickson suggest that the eldest member of Indochinese families is frequently the member of the family who decides if another family member should seek medical care and if so what type of care to seek (folk versus biomedical).[18] It is important that health care providers are aware of decision making models when a course of treatment must be decided upon, otherwise an unwillingness to consider a proposed course of treatment or a later reversal of the decision might result.[17]

Just as the opinions of significant others can be salient in making decisions about health care utilization and treatment, they can also be important in deciding whether or not a patient adheres to a given treatment. If members of the immediate and extended family support a treatment plan, better adherence to the plan is often the result.[15, 17]

Cultural differences can also emerge within the context of interactions and relationships with health care professionals. These issues go beyond simply language or communication barriers, although these too are significant sources of problems.[11, 13, 18] Although most North Americans expect their health care providers to assume a professional stance that is characterized by a distant and impersonal relationship, this somewhat detached approach to a patient might have some negative consequences for members of different cultural groups.[17] For example, Mexican-Americans and Puerto Ricans expect that their health care providers show concern for them as a person, rather than just as case. They expect that their health care provider should reduce the social distance between themselves and their patients, display "personalism," "respeto," and spend a considerable amount of time speaking with them about their health.[11] When health care providers display this type of concern, their patients feel more comfortable discussing intimate topics. Consequently, better health care can be delivered.[19]

... some of our medical procedures can be both foreign and alarming to members of other cultures.

In contrast, members of Asian cultures might exaggerate the social distance that exists between health care providers and patients. Asians often display a significant amount of deference and respect to people of a higher social status, thus they might be hesitant to ask questions of their health care providers, even if they do not understand what they are being told, or are confused about either their condition or treatment.[13, 18] Therefore, it is often important that when serving this population that medical professionals encourage their patients to ask questions and seek clarification.[13, 15]

Finally, of particular concern in a discussion of health care, child birth, and pregnancy is the status of women in cultures other than our own. In some cultures women are expected to remain close to their homes and neighborhoods, or are not given much independence from their families and husbands. Providing health care to women from these cultural backgrounds can be difficult because they are expected to subordinate their own needs to the needs of the family. Scott cited an example of a woman whose husband forbid her to leave her house during the day, thus making medical treatment nearly impossible.[16]

CULTURAL PERCEPTIONS AND PRACTICES SURROUNDING PREGNANCY AND THE BIRTH PROCESS

Different cultural groups might have different concepts about pregnancy and the birth process which will influence their encounters with our medical system, including the arenas of diet, activity during pregnancy, the norms of modesty and privacy around the childbirth, the normal physiology of childbirth, and obstetrical techniques.

Other cultures have specific prescriptions of diets that are appropriate for pregnant women. In cultures where the cold/hot classifications of food are prevalent such as Puerto Rican, Haitian, Mexican, and various Asian cultures, several foods, including iron pills and vitamins, can be considered inappropriate for pregnant women or women who have just given birth. A study of Khmer women determined that they considered pregnancy a "hot" state and therefore would not consume foods that were classified as hot such as red peppers.[20] The Hmong believe that pregnancy cools the body and women who have just given birth should eat warm foods; specifically, they believe that women should eat chicken, rice, and eggs for forty days after their delivery.[14, 22] These beliefs about diet can have real clinical implications. For example, Khmer do not regularly eat dairy products, and thus when health care providers suggest these products to pregnant women as a good source of calcium their advice is largely ignored.[20]

Cultures differ in the amount of activity that they expect and allow of pregnant and postpartum women. Hmong women believe that they should not work hard during their pregnancy and specifically, that they should not raise their hands over their heads.[22] In contrast, Hutterite women do not change their work role during pregnancy.[23] Several cultures including Mexican and Hmong mandate a forty day period of convalescence after childbirth with limited activity and special dietary restrictions, similar to those of pregnant women.[17, 22]

Different cultures expect different norms of modesty and levels of privacy surrounding the birth process. When a culture highly values female modesty, this emphasis is carried into medical encounters, especially during the delivery of gynecological and obstetrical care. For example, Mexican-American husbands have been known to request to be allowed to remain in the room when their wife was being examined in order to protect her modesty.[17]

Just as norms of modesty vary between cultures, so do norms of privacy. Some cultures believe that the entire family should attend the birth process, while others consider it a private and personal event which should only be attended by those giving birth and a midwife.[14, 23] This has huge implications for the type of care that is sought by pregnant women of disparate cultural backgrounds frequently impacting whether women seek biomedical care for their delivery.[25]

Finally, often members of other cultures do not understand or are even fearful of the medical procedures that surround childbirth in our country. For example, Hmong believe that souls become lost during sleep, and so they can be quite fearful of any procedure that involves anesthesia, especially surgery, such as cesarean section.[14] Furthermore, they are concerned that if a woman does not give birth in her husband's home or a cousin's home than evil spirits will harm the mother or child, and therefore they resist giving birth in hospitals. Mexican-Americans voice concern that cutting the umbilical cord will let in "mal aire," bad air, which can have harmful effects on the new mother.[17] Thus some of our medical procedures can be both foreign and alarming to members of other cultures.

THE ROLE OF POVERTY

A deeper understanding of issues surrounding poverty is critical for medical professionals serving immigrant populations. Women who live in poverty might lack health insurance as well as have few resources for prevention, poorer health habits, little formal education, and stressful pregnancies. A study by Hubbell et al of 652 low income women (64% Anglo, 28% Latino) in Orange County, California, found that having insurance was the strongest predictor of access to health care. Thirty-nine percent of those who did not have health care insurance lacked a regular source of care, and preventive and prenatal care were among the unmet needs of the poor population.

Lazarus' study of barriers to care in a prenatal clinic found that poor women did not understand much of the common birth vocabulary such as "dilation" or "breech" and yet most were too embarrassed or "self-conscious" to seek clarification.[29] Lazarus also found that most of the women visiting the prenatal clinic were undergoing stressful pregnancies. Twenty-two of the 53 women she met with said they were often depressed and several voiced concerns about cutbacks in Medicaid and other government assistance programs. Although this might have implications for the course of a pregnancy, these women reported that their doctors did not address these issues. Although not all minority or immigrant women have stressful pregnancies and financial concerns, it is important to consider how living in poverty might have an impact on the process of pregnancy and childbirth.

THE ROLE OF RACISM

Finally, health care providers must consider the issues of racism when serving individuals from different cultural backgrounds. It is possible that an individual's experiences with racism both in and out of the medical setting might play a role in health outcomes. It is important to be aware that people's experiences are shaped not only by cultural differences but also by racism and other social processes.[33] Likewise, Blackmore et al point out that racism is an unmeasured etiologic factor in the development of diseases. They suggest that in seeking causes for the higher rates of Black women's preterm deliveries, studies should examine these women's differential exposure to unrecognized social, political, and environmental risk factors. Furthermore, studies show that people's exposure and concomitant response to distressing situations, such as discrimination, might be a psychosocial health risk factor.[31, 34] Further investigations are therefore needed with special attention to intra-ethnic variation and particularly, the gender-specific aspects of racism.[31]

Finally, women's previous experiences of racism might contribute to a certain amount of lack of trust for medical professionals thereby making the delivery of health care more difficult. Levy argues that Blacks do not know how they will be received by Whites in new situations and that their past experiences of humiliation and discrimination produce feelings of anxiety and resentment.[30] Furthermore, some individual's become convinced that experiences with White institutions are "all powerful and that relationships with them most often end in frustration."[12, 30, 35] This inclination not to trust individuals and institutions of another culture might negatively impact a minority patient's rapport and communication with health care providers. Levy suggests that Black patients might even resort to concealment or disguise when communicating with White medical professionals.[30]

RECOMMENDATIONS

Given this list of issues, what can be done to improve the quality of care to members of different cultural groups? First, we must be willing to recognize the complexity of these issues and to engage in an ongoing discussion of how issues of cultural background, race, and ethnicity intersect with the delivery of health care. Second, we must keep our understanding of these issues fluid; we must look for intra-ethnic variation as a function of the patient's level of formal education, generational removal from immigrant status, association with ethnic and family network, prior experience with medical services and childbirth, their age at immigration, their residential background (urban versus rural), and their patterns of migration (i.e., back and forth migration to motherland). Although one's beliefs about child birth might be impacted by an individual's cultural background, the variables listed above will modify the extent to which one's cultural background will impact their interactions with the health care system.[15]

It is exceedingly important that health care professionals use good interpreters. The use of an inappropriate interpreter can exacerbate all of the above listed sources of cultural conflict.[13, 18] The use of family members or interpreters not trained in either cultural or medical terminology should be avoided[13] Yet, it is just as important for health care providers to be aware of nonverbal communication norms that are specific to each culture. By being aware of such areas as pauses of silence, physical distance, eye contact, emotional expressiveness, and body movements it is possible to avoid misunderstandings and unintentional offenses.[13]

In summary, two points should be stressed. First, all health care professionals should strive to become culturally sensitive and competent when working with populations from different cultural backgrounds. Cultural competence and sensitivity requires health care providers to consider a number of different areas: verbal and nonverbal communication, conceptions and beliefs about health, the etiology of sickness, expectations of interactions, the importance of the role of family members in decisions, and the impact of racism and poverty. Finally, it is helpful for health care professionals to work with members of the communities including healers, informants and partners in health care delivery. As Scott points out, these cultural traditions, though possibly running counter to our own cultural understanding of disease and treatment, have survived for generations and may be actually effective.[16] In the very least, if a health care provider does not have a knowledge or connection with the different cultural communities served, he/she runs the risk of compromising the care delivered by alienating patients, or fostering a lack of compliance with preventive or indicated medical care.

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Theoretical Perspectives on Violence and Youth

Fayneese Miller, PhD and JoLee Webb

A recent article on youth in The *New York Times* reported that young people are very concerned about violence. Specifically, they are concerned that they will be victims of a violent act such as homicide or assault. Although homicide is the second leading cause of death for youth in the United States, most young people will never encounter either homicide, suicide, abuse, or accidents. Those who are likely to encounter this violence are boys between the ages of 15 and 19.

The purpose of this paper is to discuss the incidence of exposure to and the perpetuation of violence among young people. Although African American males are the main focus of this paper, they are by no means the only group for which violent behavior is a problem. There has been an increase in violent crimes and deaths across racial or ethnic groups. For example, according to the February 1995 Governor's Justice Report on Juveniles in Rhode Island, the violent crime rate for youth under the age of 18 increased 148%. Firearms were involved in 60% of the deaths for Rhode Island youth. In 1987, the arrest rate for Asian Americans who commit violent crimes rose from 10 to 172 and from one or two for Native Americans to 70. Rhode Island statistics for White males were not available. However, according to national reports, the rate has increased significantly among White males as well.

THEORIES EXPLAINING VIOLENT BEHAVIOR AMONG YOUTH

Several theories have been put forth to explain the incidence of violence among African American males. One theory, the subculture of violence, postulates that there are community norms that support the use of aggression or violence to resolve such problems as challenges to one's sense of manhood.[1,2] A second theory, economic deprivation, attributes violence to frustration from a lack of desired material resources, stimulating feelings of resentment, hostility, and aggressive impulses.[3,4] This is the explanation most often used to explain the behavior of youth who kill or threaten other youth over their jewelry, sneakers, or jacket. According to a third theory, the structural cultural, maladaptive responses, like low self-esteem and self-hatred brought about by exposure to racism, lead African American males to commit violent acts.

Each of these theories have shortcomings. The subculture of violence theory is circular, fails to acknowledge the role of social problems or issues like poverty and discrimination, and over predicts the number of African Americans who are likely to commit violent acts.[5] The major criticism with the economic deprivation theory is that it only attempts to explain the behavior of African Americans who are poor and commit crimes and not of those who are poor and do not commit crimes. The self-esteem of African Americans who commit violent crimes is not necessarily low. The structural-cultural theory is therefore also not without problems.

An alternate theory to those more often cited as explanation for violent behavior among youth is the social adaptation theory of alienation and hopelessness. According to this theory, young people who perceive the world as "this is the way it is and always has been" are more likely to engage in violent acts than those young people who think they can change the world.[6] Young people who are unable to perceive themselves as affectors of change are more likely to have a stable alienation, less likely to have a future orientation, and less likely to be hopeful about their future. For young people who are alienated, hopeless, and without a future orientation, engagement in violent behavior may provide a sense of power, albeit superficial and destructive, and belongingness. Often, alienated youth are also very likely to be members of gangs or close-knit cliques, to come from chaotic or disorganized environments, and to be users or sellers of drugs or alcohol.

Currently, there is no one theory that explains the high incidence of violence among African American males. The public health framework that recognizes host, agent, and environment may hold promise. This framework is interactive and includes personal, social, and cultural factors which may contribute to the problem.

PUBLIC HEALTH PERSPECTIVES ON VIOLENCE

According to Hammond and Yung, "the host is the person whose behavior may determine or contribute to the problems.[7] The agent is the facilitating physical mechanism(s) (e.g. in the case of a disease, the pathogen). The environment incorporates the broader social, institutional, cultural, and physical forces that might inhibit or support the onset of the problem."

The host explanation for violent behavior among African American males suggests that psychosocial or biological factors may contribute to youths' risk for becoming a victim or perpetrator of violence. The host centered psychosocial risk factors that have been identified are perceived aggressiveness by peers, belief that aggression increases self-esteem, peer rejection, and exposure to familial violence.[8-13]

Biological risk factors of head injuries from falls and injuries have been proposed as correlates for violent behavior.[14] Alcohol and drug use have also been identified as risk factors. Dawkins and Dawkins found that there was a stronger association between drinking and violent offenses for both male and female African American youth who engage in anti-social or violent behaviors than White or Latino youth.[15]

Firearms, which are an example of an agent, contribute to 60% of the homicides that occur in the United States. In a six year study of relationships among handgun regulations, assault, and homicide patterns, Sloan et al. found that the high incidence of risk for injury or death by firearms in Seattle was due to that city's concealed weapons policy.[16] Several states in the United States have instituted right to carry arms policies, but the long-term effects on the incidence and prevalence of violence in those states have yet to be determined. A recent incident in Texas, although it does not involve youth, speaks to the potential for increased use of firearms to resolve conflict. Two young men had a minor traffic accident, one pulled out a gun and killed the other. The young man who fired the gun was described as working class. Owning and carrying a gun might symbolize power for an individual who often feels powerless in other social or economic ways.

Poverty and inner-city residence have been proposed as environmental factors that influence the incidence of violence among youth. Past studies have shown that urban youth of low socioeconomic background are more likely to carry weapons, witness violence, or engage in fisticuffs than suburban youth. Shakoor and Chalmers studied African American eighth graders living in an extremely violent, low income neighborhood in Chicago.[17,18] They found that 55% of the boys and 45% of the girls in the study had seen someone shot. Economic status, in and of itself, does not account for the high incidence of violence in urban areas. Community disorganization or chaos, unemployment, high mobility, family dysfunction, and population density coupled with poverty help explain the high incidence of violence in urban areas. In addition, feelings of alienation and hopelessness, which are linked to the conditions listed above, contribute to violent behavior.

In summary, a focus on such factors as host, agent, and environment factors encourage a holistic perspective and interactive approach to the problem of understanding, explaining, and preventing violence among young people. What is important to note about the public health approach is that it is interdisciplinary and therefore allows for a more comprehensive approach to understanding and, ultimately, combating violence among youth.

Pubic Health and Statistics on Violent Crime Among Youth

Although a public health approach to violence prevention has been suggested by many social scientists and medical professionals, caution is warranted. The state of knowledge in this area is still underdeveloped.[19] This, however, has not deterred the public health community from urging immediate action. In 1986, for example, the National Medical Association called for the legitimization of violence as a public health issue for physicians. The Department of Health and Human Services, in a report entitled *Health People 2000*, targeted the year 2000 for achieving a goal of significant homicide reduction for African American males between the ages of 15 to 34.

The majority of violent crimes by African American males occur between the ages of 15 to 34. Crime statistics reported by the Federal Bureau of Investigation, however, show a significant jump in violent behavior, regardless of race or ethnicity, around the age of 15. In 1993, the number of males who committed murder rose from 284 for 10-14 year old males to 4,428 for 15-19 years old. The number of murders committed by 20-24 year olds during that same year was 2,459. The same pattern was reported for females; 10-14 year olds committed a total of 34 murders and 15-19 year olds committed 219. The number of murders recorded for 20-24 year old females showed an opposite trend than males. The number increased by more than 65% African American males between the ages of 15-19 had a greater increase in the number of murders than any other racial/ethnic group.

> *Why is early to middle adolescence a critcal time for youth? What kind of interventional programs are needed for this early group?*

Suggestions for Future Directions

Given the age at which a large number of violent crimes tend to be committed by youth, a focus on developmental trajectories and outcomes for youth is needed. Why is early to middle adolescence a critical time for youth? What kind of interventional programs are need for this early group?

Erik Erikson proposes that children and youth have to resolve conflicts at various stages of development. For youth, he proposes the conflict involves feelings of industry versus inferiority and identify versus role conflict. Youth who are unable to resolve conflict will feel inferior and experience role confusion. Youth who are unable to resolve conflict may be more vulnerable to peer pressure or have a higher need to please or affiliate. These youth may also be more likely to feel alienated and hopeless about their future. African American males have been identified as the group most at risk for violent behavior. Are they more likely to feel inferior and experience role confusion than others? What happens to young African American males prior to and at the onset of puberty that might affect the way in which they come to view their sense of worth and ability? What role do teachers and members of society have in influencing the incidence of violence among African American males?

African American males are more likely to be retained in the early school years and to have lower levels of achievement motivation than other students. According to our research on alienation and hopelessness among minority males, African American and Latino males who are alienated from school and who have no school social supports are at risk for recruitment into gangs with involvement in anti-social behavior. African American males, in general, are more likely to experience avoidance behavior on "Main Street". (That is, when young African American males walk the streets people cross the street in order to avoid contact.) The message sent by such behavior is "I am afraid of you. You are going to rape, rob, or murder me." or "I don't think much of you." The lack of respect for these males is painfully obvious. This is the one incident, other than being suspected of planning to steal and therefore being followed around in a store, that young males in my research frequently report as devastating events in their lives. One could speculate that the lack of respect shown by other leads to a lack of a development of a health self-respect.

The illusion of power or control that results from continued exposure to avoidance behaviors might have some influence on the behavior of African American males. In order to prevent the illusion of control and the resulting violent behavior of some African American males, an appreciation of the fact that African American males are not homogeneous and an understanding of the contributor effects of prejudicial attitudes and biased treatment on behavior needs to be acknowledged and addressed.

Psychological research can be used to focus on the "intrapersonal contexts of a particular behavior problem".[7] Psychological research is therefore useful in the identification of behaviors related to violence, research design, and evaluation of violence prevention programs. In order to combat the problem of violence among youth, politicians, educators, researchers, community agency personnel, and neighbors will have to acknowledge that violence is a public health issue. African America males are not inherently evil, nor is there developmental abnormality. Something happens along the path of development, however, that leads some African American males to stray from the "normal" paths of moral and social development. The task for researchers is to identify those factors which lead some African American males to follow a different path of development and to develop intervention strategies which lead to positive rather than life ending consequences such as death.

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Telling Time

He took my hand.
He said he could no longer stay
where clocks made no noise.
Then he sat down and died.

I did not let go
until his skin turned cold.
This too was quiet.

I appealed to physics.
I ran to his house
with the old clock which ticked
because gravity sucked
at lead weights
suspended from its gears.

He had taught me to rewind them.
He said it would work when he was gone,
and to keep it wound.

– Ron Willy

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AIDS and Minorities

Alvan E. Fisher, MD and Rinchen-Tzo Emgushov, MD

The CDC recently stated that over 500,000 cases of AIDS have been reported in the United States as of October 31, 1995, with half of these being diagnosed since 1993.[1] Though AIDS remains stereotypically associated with homosexual white men it has somewhat silently become a disease disproportionately affecting racial and ethnic minorities in the United States. Indeed, AIDS case rates are currently six-fold higher for African-Americans and three-fold higher for Hispanics than for whites. During the first six years of the AIDS epidemic in the U.S. (1981-1987) 50,352 cases were reported; of these 25.4% were African-Americans and 14% Hispanics with 60% whites. Since 1993, 38% of reported cases have been African-Americans, 18% Hispanics, and 43% whites. A majority of cases on an annual basis have been reported in African-Americans and Hispanics since 1992.[1] This dramatic shift in the racial and ethnic epidemiology of AIDS has occurred primarily in urban settings and especially in the Northeast states.

The associated risk factors for HIV acquisition among reported cases in the U.S. have also shown a dramatic shift from the early years of the epidemic. The proportion of cases among individuals reporting injecting drug use (IDC) increased from 17% during 1981-1987 to 27% during 1993-1995. Similarly, the proportion of cases attributed to heterosexual transmission increased from 3% to 10%, while the proportion of cases among men who have sex with men decreased from 64% to 45%.[1] This shift in the HIV exposure categories to greater proportions of injection drug users and heterosexual transmission cases has also affected blacks and Hispanics disproportionately and most dramatically women.

In 1993 racial/ethnic minorities accounted for 75% of all cases of AIDS in women and 84% of all cases in children.[2,3] IDU was the most common exposure mechanism among women with AIDS from racial/ethnic minorities accounting for 47% of cases. Heterosexual transmission accounted for an additional 37%, but half of these were in women whose heterosexual contacts were associated with IDU.[3] Thus, at least two-thirds of AIDs cases in women from racial/ethnic minorities in 1993 were either directly or indirectly related if IDU.

Among men with AIDS from racial or ethnic minorities male-male sexual transmission accounted for 39% of cases and IDU 38% in 1993 compared to 71% and 11% respectively for whites.[4]

HIV infection is increasingly associated with unemployment, poverty and illiteracy, all of which correlate with decreased access to health education, preventive services and medical care.

In Rhode Island over 1,500 people have been diagnosed with AIDS - the eighth highest per capita state incidence in 1995.[5] Rhode Island has reported the ninth highest total number of cases of AIDS in women. In the U.S., the HIV exposure categories of IDU and heterosexual transmission have increased faster than any other risk category and in R.I., IDU accounted for 41% and heterosexual transmission 19% of all cases in 1994 (versus 33% and 7% respectively of all R.I. cases prior to 1990). That same year IDU accounted for the direct route of transmission for 56% of women with AIDS in R.I. and heterosexual transmission 39% with a substantial proportion of the latter acquiring infection from male injection drug users.6. Racial/ethnic minorities have been disproportionately affected by AIDS in R.I. African-Americans and Hispanics account for 35% of adult cases in R.I. and 67% of pediatric cases, though these communities represent approximately 10% of the population.[6]

HIV infection is increasingly associated with unemployment, poverty and illiteracy, all of which correlate with decreased access to health education, preventive services and medical care.[7] In 1992, 33% of African-Americans and 29% of Hispanics lived below the federal poverty level compared with 10% of whites.[8] The social, cultural, and economic factors that affect racial and ethnic minorities in the U.S. have had a major impact on the risk, transmission of, and community response to HIV infection.

From the earliest years of the AIDS epidemic, stigmatization has been present forcing many gays further and deeper in the closet while others have become vocal and visible activists. There is a tendency in the U.S., especially in the media, to "conceive of homosexuality in largely male, middle-class and, above all, white terms."[9] Black gays are and have been in many communities subject to de facto segregation from other gays; "racism has always been alive and well in the gay world."[10] In addition, "concern over AIDS seems to have failed to mobilize black, Hispanic an Asian gays."[9] Few role models from minority communities have stepped forward and when they have (such as Arthur Ashe and Magic Johnson) they have frequently distanced themselves from association with AIDS organizations perceived to be gay-oriented.[11] The experience of Haitians in the U.S. in the early years

ABBREVIATIONS USED

AIDS	Acquired immune deficiency syndrome
CDC	Centers for Disease Control
CIA	Central Intelligence Agency
HIV	Human immunodeficiency virus
IDU	Injected drug use

of the epidemic, when their national and racial origin alone was considered a risk factor for AIDS, clearly reflected the stigmatization that AIDS produces in minority communities.[9] This experience certainly did not encourage other people of color to become active in the early fight against AIDS. Indeed, the majority of community-based organizations dedicated to AIDS have been founded, funded and directed from within mostly white homosexual communities even as the epidemic has increasingly affected heterosexual members of racial/ethnic minorities leading to inevitable philosophic and political conflict within many of these organizations.

The recent experience with Kemron demonstrates how racially polarized the U.S. has become with respect to AIDS. Kemron is a oral preparation of low doses of alpha-interferon that was touted not only as an AIDS treatment but as a possible cure by a Kenyan physician and the Kenyan government in 1990. Some members of the African-American community in the U.S. created a furor with charges of racism directed at the medical and scientific establishment over the lack of testing and availability of Kemron in the U.S.[12] However, the data supporting this product was far from convincing being anecdotal, uncontrolled and scientifically unsound. The Amsterdam News, the largest African-American newspaper in Ne York City, was responsible for much of the reporting on Kemron and continued to tout its value even after further reports from Africa and two trials in the U.S. failed to demonstrate any benefit.[13] The charge of racism certainly had historical merit given the historical record of institutionalized racism involving the scientific and medical establishment. The experience of the so-called Tuskegee experiment in which poor black men with syphilis were denied treatment in order to complete a decades-long natural history study helped to define this attitude and led to further denial of the realities of HIV infection and AIDS.[14] In a recent interview in Providence, Tony Brown, the African-American commentator and for twenty years host of 'Tony Brown's Journal' on the Public Broadcasting System demonstrated some of these attitudes regarding AIDS. He declared that "the AIDS epidemic is a scam...no one has proved that HIV causes AIDS. ...They have told a lie...and will not admit a lie." He described the CDC as the "medical establishment CIA." He further explained that "fear and scam only work because they chose groups that are disliked [gays and blacks]."[15]

HIV infection and AIDS continue to spread in the U.S. Every city, every state and every community has felt its effects. At the middle of the second decade of AIDS much has been learned about the virus, its epidemiology, its medical consequences and its treatment. Much still needs to be learned in order to disseminate all of this knowledge throughout the U.S. and contain this epidemic. AIDS in many ways reflects and magnifies many of the problems of our society: racism and homophobia, a health care system in need of many reforms, an unwinnable war on drugs. It is ironic and unfortunate that these problems continue to interfere with the war on the AIDS epidemic even as much progress has been accomplished.

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Managed Care: Minorities and the Poor

Stanley Hoyt Block, MD

HISTORY

Although managed care has swept across the country, bringing enormous changes in the way that millions of Americans receive care, many minority communities were generally unaffected by these changes---until recently.

Some members of minority communities were excluded from managed care for a variety of reasons. First of all, many people in inner-city areas are covered under Medicaid--the federal program for poor Americans, which until recently, has been run in most areas on a fee-for-service basis. Secondly, many inner-city Americans who had access to health insurance through their employer found that HMOs were not interested in enrolling what was perceived as a high-risk, high-utilizing population in the heart of America's poorer cities.

Some HMOs feared that the incidence of costly diseases, such as AIDS, tuberculosis, and lead poisoning were all too frequent in minority communities and that tragic and expensive complications of violence, drugs, and prematurity could bankrupt an HMO. Furthermore, there has been a perception, though not an accurate one, that poor and minority Americans sue for malpractice more than their more affluent suburban neighbors.

How did those HMOs with such concerns avoid enrolling minority communities? They often used a variety of methods, including advertisements that were clearly geared to the more affluent, working well, the avoidance (or red-lining) of entire inner-city districts when doing public relations and enrollment efforts, and the lack of interpreters which prevented some minority communities (including Spanish, Cambodian, Hmong, Lao, Vietnamese, Cape Verdean, and Haitian speaking patients) from enrolling even if they wanted to.

ABBREVIATIONS USED

AFDC	Aid for dependent children
AIDS	Acquired immune deficiency syndrome
HMO	Health maintenance organization

Against this rather sad backdrop, it should be mentioned that certain HMOs refused to acquiesce to economic or social discrimination and felt that reaching out to minority communities was their public obligation and social trust. They should indeed be commended.

A CHANGING ENVIRONMENT

As managed care enrolled millions and millions of working, middle-class Americans, many States looked to the concept of managed care as a method of controlling their ever-increasing Medicaid costs for the poor. Medicaid spending had been rising at an annual rate of over 20% between 1988 and 1992, and accounted for more than a quarter of many states' budgets this past year. In order to get around the original 1965 federal legislation that guaranteed Medicaid recipients freedom of choice of physicians and hospitals, waivers had to be obtained from the federal government by each state entering into a compulsory Medicaid managed care program. Such waivers have been obtained by numerous states, including Rhode Island.

As states were obtaining their waivers to convert Medicaid programs from fee-for-service to managed care, some managed care organizations were finding increasing competition in enrolling new members. Some areas were "saturated" with HMOs, and competition for members became fierce. In certain cities, most of the "working well" were already signed on to a variety of HMOs, and competitors needed new markets. This led to a new interest in previously uncapitated communities, such as Medicaid recipients, inner-city residents, and minorities. A historical lack of interest in such "high risk" communities was coming to an end.

In 1993, Rhode Island was granted such a waiver from the Health Care Financing Administration, the federal agency responsible for administration of the Medicaid Program. This waiver enabled Rhode Island to develop a statewide managed care project known as RIte Care, which includes almost all families and individuals receiving AFDC and RI Medical Assistance. The aged, disabled, and blind are excluded and remain on the previous Medical Assistance Program. Through RIte Care, eligibility for Medical Assistance was expanded to include all uninsured low income children under six and pregnant women in the state. Also, a buy-in provision assured that all uninsured children under the age of six in RI could have access to this program. All RIte Care patients have been enrolled on a captitated basis in one of five participating HMOs: United Health Plans of New England, Inc., Neighborhood Health Plan of Rhode Island, HMO-RI, Harvard Community Health Plan and Pilgrim Health Care.

THE BENEFITS

HMOs have significantly reduced the rate of increase in the cost of medical care to many segments of our society. Can managed care do the same for the Medicaid population? With the failure of national health care reform, states are banking that competition among managed care organizations will lead to better service for the poor at a lower cost than the previous fee-for-service models. It is felt by many that market-driven solutions will provide some financial relief to the ever increasing costs of providing care to the 13% of Americans who utilize Medicaid.

It is hoped by some that medical care will not only be cheaper but better under a managed care model. If patients can be encouraged to utilize ambulatory facilities instead of expensive emergency rooms, much money can be saved. If alternatives can be found to lengthy hospital stays (sometimes for serious social rather than medical reasons), then huge savings can be achieved. Appropriate immunizations given in a timely manner can prevent many diseases that otherwise cause devastation in our pediatric population. For example, Haemophilus influenzae meningitis, once all too common, is now becoming almost unheard of in properly immunized children. By emphasizing preventive and primary care, many dollars can be saved by the HMOs (and states), while providing better care to the poor and inner-city patients. It's certainly less expensive to track immunizations and to call parents up (via a translator if needed) when their children's immunization appointments are missed, than it is to treat a full blown case of meningitis in-hospital for one or two weeks or more. As states save money, additional low-income citizens can be "insured" under such managed care programs, thus bringing health care access for all Americans closer to reality.

QUESTIONS

Until recently, most experience in Medicaid managed care has been with voluntary enrollment, which may well have achieved a more compliant membership population. Can the same be achieved with mandatory enrollment? As more noncompliant members are enrolled, will the same benefits accrue? More dollars may be needed to be invested in outreach efforts, translators, and social service. Innovative methods may be needed to enhance compliance, such as home visits, school based clinics, and the recruitment of culturally sensitive and linguistically capable staff. Since only 38% of Rhode Island's Medicaid population (the aged and disabled), who are often in long term nursing-home care, utilize 78% of the Medicaid dollars, while 62% of the Medicaid population (mainly women and children on AFDC) utilize only 22% of the dollars, can Medicaid managed care programs that address only the latter group effect significant savings overall?

One of the basic tenets of managed care is that the cost of up-front preventive care will almost certainly bring both financial and medical rewards, i.e., a healthier patient population and a healthier "bottom line" to the HMO, as well as financial savings to the state. Will this combination hold true for mandatory Medicaid managed care populations? This remains to be seen. However, a major concern is that patients go "on" and "off" of the Medicaid rolls so frequently that the cost to the HMO of good preventive care (such as immunizations, outreach efforts, lead screening, nutritional services, genetic counseling in several different languages, etc.) may only "pay off" if the patient remains with that HMO for several years---an unlikely event in many areas. If high quality preventive care is not cost-effective" because the patients drop out of the HMO before the benefits can be seen, then one of the major tenets of managed care will unravel rather quickly for HMOs serving the Medicaid population.

> *More dollars may be needed to be invested in outreach efforts, translators, and social service. Innovative methods may be needed to enhance compliance, such as home visits, school-based clinics, and the recruitment of culturally sensitive and linguistically capable staff.*

THE RISKS

Prior to the interest of HMOs in the inner-city population, certain "essential community providers" such as community health centers and inner-city hospitals shared in the provision of care to needy, minority, and non-English speaking Americans. Such providers generally served poor patients because they wanted to; it was part of, or even their main mission. They were part of the community and stayed with the community for decades.

These essential community providers have struggled to break down the barriers to primary care, including lack of transportation for poor patients with no cars, the fear of being docked when hourly employees visit the doctor during the daytime, inability to speak English, and the traditional overuse of the emergency room by many inner-city residents as a source of ongoing primary care. Community health centers have established free patient vans to bring families to the health center, started evening hours for the working poor, and hired on-site translators to break down the language barriers of immigrants needing health care.

As HMOs became interested in this new market, nationwide the track record has not always been exemplary. In Minnesota, there have been accusations of Medicaid HMOs skimping on cancer screening tests for poor women. Patient tragedies have been documented in Tennessee when their Medicaid managed care program (TennCare) was forced upon an unwilling private sector. For many, TennCare brought more rather than less bureaucracy. Disruptions in care, requiring changes in providers, and enormous distances to one's "medical home" increased the severity of illness in many cases, resulting in death on at least one occasion, according to many reports. Some HMOs, eager to make a quick profit, allegedly signed up more patients than they could possibly handle, and claimed providers who were unlicensed or dead. According to a newspaper article (A Free-for-All in Swapping Medicaid for Managed Care- NY Times Oct. 2, 1995), there have been reports in many states of "...sales people steering clear of potential applicants who looked as if they would require costly medical services." Reports of tragedies because of lack of translators have surfaced for non-English speaking clients trying to access English-only speaking HMOs. Political leaders in some states have claimed that these are the growing pains of rapid change in the medical environment, but one wonders whether such pains should be born by the most vulnerable segments of our society. Certainly, the FDA requires drugs to be proved safe and effective before release; should we expect that medical systems should be changed for the poor before their safety has been proved?

A Bright Future?

Many essential providers in inner-city America have vast knowledge and experience in bringing medical care to poor, minority and non-English speaking Americans. They bring decades of knowledge in how to motivate difficult-to-reach populations to seek care, and to improve health. They know all about inner-city diseases including lead poisoning, tuberculosis, sexually transmitted illness, domestic violence, and more. Culturally sensitive, bilingual staff for various immigrant populations have been crucial to such providers in bringing medical care to inner-city America for decades. However, such essential providers, including some inner-city hospitals and the over 800 community health centers nationwide which provide care to more than 8 million needy and minority Americans, often have lacked financial resources and even business experience to improve their infrastructure.

With the interest of major managed care corporations in the inner-city areas, under Medicaid managed care programs, there is a real hope that the business acumen and financial capital of corporate America can be combined with the dedication and enthusiasm of the traditional providers of inner-city care, to greatly improve the lives and health of millions of poor and minority citizens.

In Rhode Island, the fourteen community health centers have formed an HMO (Neighborhood Health Plan of RI), with financial backing of an HMO in Massachusetts, to provide care under RIte Care----the state's Medicaid managed care program. The fourteen community health centers are also participating in RIte Care through major regional HMOs. This cooperation brings with it the real hope that the infrastructure of inner-city health care can be improved. If funding can be found to expand the hours and days of operation of the fourteen community health centers, vast savings can accrue decreasing emergency room visits and even hospitalizations. In some states, legislatures have allocated the resources needed to improve the infrastructure of community health centers as they enter the managed care arena; this has not been possible in Rhode Island. Yet, low capitation rates and huge numbers of uninsured make such funding necessary. Will the private sector be willing and able to invest in the community health centers? Will the health centers survive in the present economic climate? Will the states look at Medicaid managed care merely as a method of saving money rather than of improving health? Will we see capitation rates well below dollars needed to bring good medical care to inner city and minority Rhode Islanders? Or will we see a very bright future in which the expertise, experience, and financial capital of private managed care organizations is combined with the dedication, commitment, and multi-linguistic resources of our community health centers to bring a remarkable improvement in outreach and delivery of care to poor and minority Rhode Islanders?

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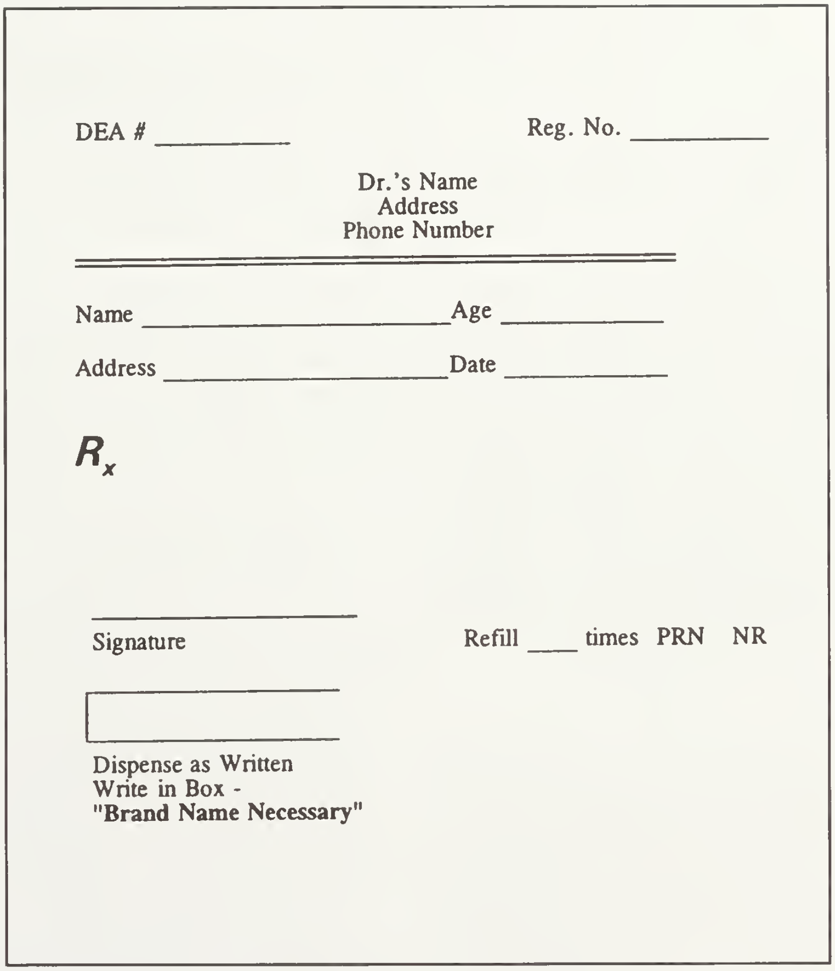
Physician/Patient/Pharmacist Relationship

Mario Casinelli, Jr.

Mr. M. Casinelli is chairman of the Rhode Island State Board of Pharmacy

What the pharmacist should expect from the physician:

1. **Prescription orders are to be written on the *new prescription blank* as mandated by law. This will eliminate questions and phone calls.**
2. All control prescriptions must have the patient's name, address and date, along with the DEA number. The maximum quantity for schedules III-V is 100 dosage units. For Schedule II, the maximum is a 30-day supply, up to a maximum of 250 dosage units.
3. When medication is written for a condition other than official indications, the pharmacist should be notified.
4. When available, a physician's back phone number, and fax number, would be desirable. Instructions such as "as directed" or "prn refill" are not desirable.
5. Multiple prescription blanks can be a problem, since they are not recognized by the Division of Drug Control. Control medications must be written on a separate blank.
6. When a pharmacist asks to speak with a physician, a response should be forthcoming as soon as the physician is free.



DEA # ________ Reg. No. ________

Dr.'s Name
Address
Phone Number

Name ____________________ Age ________

Address ____________________ Date ________

R_x

Signature

Refill ___ times PRN NR

Dispense as Written
Write in Box -
"Brand Name Necessary"

What the physician should expect from the pharmacist:

1. First and foremost, the prescription orders for the physician's patients should be filled exactly as written. If there is a question or changes required, the physician should be notified and documented on the hard copy.
2. The pharmacist should provide the physician with a back line phone number and fax number, if available.
3. The pharmacist should notify the physician if the patient is not complying with the physician's orders.
4. The pharmacist should notify the physician if there would be serious drug interactions with medications in the patient's profile.

What the patient should expect from the pharmacists:

The patient is, at all times and under all conditions, entitled to courtesy, consideration, and professional and dignified counseling.

Public Health Briefings

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Judith Feldman, MD, MPH, and John P. Fulton, PhD

Chronic Disease Prevention Among Minority Groups: Problems and Possibilities

Pheamo R. Witcher, MCP, John P. Fulton, PhD, Nancy Beauchene, MS, RD, Elizabeth Harvey, MD, and Becky Bessette, MS, RD

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Chronic disease prevention is a major public health priority. In Rhode Island, among 50 public health objectives selected for the year 2000, 11 were selected to reduce the burden of cardiovascular disease, cancer, and diabetes on the Rhode Island population. Much of this burden is related to cigarette smoking, excessive fat in the diet, and insufficient physical activity. Reducing these risk factors is a major goal of chronic disease prevention programs.

Public health agencies (PHAs) cannot go it alone. They do not have the staff for labor intensive interventions, and they do not have easy *entre* to the populations at highest risk of chronic disease. Based on careful surveillance, PHAs must identify community based organizations (CBOs) and health care providers with access to target populations, enlist them in health promotion activities, and help coordinate their efforts to assure efficient use of scarce resources. In short, public health agencies must engage in effective community organization to reduce chronic disease risk factors and ultimately, the burden of chronic disease itself.

> *Physicians can make a difference with minority patients by reporting correct race and ethnicity data in all medical records, by communicating simple, consistent, and culturally specific prevention messages, by checking to see that patients understand important health risks, and by assuring that patients are screened appropriately for chronic diseases.*

Abbreviations Used

PHA	Public Health Agencies
CBO	Community based organizations
BRFSS	Behavioral Risk Factor Surveillance System

Four problems hinder this process when it is applied in the minority community. First, surveillance of chronic disease risk factors in the minority community is usually inadequate for effective planning. Second, many leaders in the minority community (and therefore many CBOs in the minority community) have priorities for public health which compete with addressing chronic disease risk factors. Third, collaborations among PHAs and CBOs in the minority community are fragmented by the diversity of the minority community itself. Fourth, most PHAs and most CBOs in the minority community have inadequate infrastructure to support effective collaborations in health promotion.

Inadequate Surveillance

PHAs use a number of data sources to observe health risks, public health processes, and health outcomes in the population at large, including vital records, reports of medical encounters and disease, and sample surveys. Traditionally, PHAs have collected these data from the population as a whole. Because each minority population usually represents a small proportion of the whole population, this broad brush approach yields too few vital records, reports, or survey responses for precise statistical measurement of the minority populations.

In some cases, vital records and other reports must be aggregated over ten years or more to accumulate sufficient numbers for precise statistical measurement in a minority population. This is a frustrating process because new statistics are available only at long intervals, and year-to-year trends in health measures, except for the most dramatic, are impossible to observe.

Surveys, where appropriate, can achieve precision of statistical measurement immediately, but only by increasing the numbers of minority respondents, and therefore cost, dramatically. These extra dollars are rarely available, and must compete with intervention dollars. In addition, sample surveys of minority populations frequently miss those at greatest risk of disease and disability, because they do not have sufficient resources to reach

Table 1
Age-adjusted mortality rates[a] from major chronic diseases among white and minority groups, by underlying cause of death, United States, 1990

Indicator	White American %	African American %	American Indian/ Alaskan Native %	Asian/ Pacific Islander %	Hispanic American %
Ischemic Heart Dis.	177.4	180.7	104.0	93.7	181.2
Stroke	48.5	76.0	33.3	45.8	47.4
COPD	32.6	24.8	21.5	15.8	22.6
Diabetes	15.9	35.7	30.3	12.4	28.3
Cirrhosis	9.4	14.5	21.2	4.7	19.0
Lung Cancer	54.0	67.5	27.9	26.8	35.6
Colorectal Cancer	20.6	26.6	10.1	12.6	18.2
Breast Cancer	16.3	19.5	6.6	6.5	13.9
Cervical Cancer	1.1	1.8	0.7	0.5	0.9
Prostate Cancer	10.7	23.5	5.8	6.0	10.2
TOTAL	386.5	470.6	261.4	224.8	377.3

a - Age-adjusted to the 1980 U.S. standard population, rate per 100,000 persons
Source: CDC, NCHS, National Vital Statistics Systems, 1990

respondents made inaccessible by frequent moves, lack of telephones, and language and literacy barriers. These problems beset even the best federally-sponsored surveys and censuses.

Tables 1 and 2 demonstrate inconsistencies not infrequently observed in minority data which may be attributable to problems in reaching survey respondents at greatest risk of disease and disability. For example, African Americans have the highest lung cancer mortality rate of all groups observed (Table 1), but apparently smoke no more than white Americans and considerably less than native Americans (Table 2). Similarly, African Americans experience substantially higher cirrhosis mortality than white Americans (Table 1), but apparently drink alcohol less freqently than white Americans (Table 2). Also, native Americans and Hispanic Americans experience more than twice the cirrhosis mortality of white Americans (Table 1), but apparently drink alcohol only a little more frequently than white Americans (Table 2).

These striking inconsistencies may be attributable to one or both of two problems with data collection. On the one hand, the mortality rates in Table 1 may have been overestimated by undercounting minority groups in the 1990 U.S. census of population (a well established problem). Census data are used in the denominators of mortality rates and would inflate them if the groups in question had been undercounted. On the other hand, the frequencies of certain risk factors in Table 2 may have been underestimated by missing minority individuals at greatest risk of lung cancer and cirrhosis mortality in surveys run as part of the Behavioral Risk Factor Surveillance system (BRFSS). The BRFSS uses random digit dialing to contact potential survey respondents by telephone, a technique which is known to exclude individuals of lowest income.

COMPETING PRIORITIES

Many leaders in the minority community have priorities for public health which compete with addressing chronic disease risk factors. Of 21 health objectives ranked in order of importance by African American leaders across the U.S., for example, "reduce tobacco use" ranked between eighth and thirteenth, "improve nutrition" ranked between ninth and twelfth, and "increase physical activity and fitness" ranked fourteenth or fifteenth (Table 3). In Rhode Island, representatives of the minority community ranked "promoting healthy lifestyles" fourth or fifth among seven public health objectives (Table 4).

This is not to say that these priorities are inappropriate. The public health objectives selected as high priorities by the groups observed would, if achieved, save many lives, including many young lives, in the minority community. They would also, if achieved, prevent much family dysfunction and dissolution. In short, leaders of any community beset with the health problems of African Americans nationally or minorities locally might have ranked public health objectives much in the same way as they are ranked in Tables 3 and 4. Nonetheless, given the scarce resources available to address public health objectives in the minority community, little attention may be paid to essential chronic disease risk factors if resources are allocated according to the priorities indicated.

DIVERSITY

Collaborations among PHAs and CBOs in the minority community are fragmented by the diversity of the minority community itself. This diversity is complex throughout the U.S., especially in urban settings like Rhode Island's, which draw migrants from other American communities and immigrants from other nations. Broad racial groups include a wide variety of social groups distinguished by socio-economic status, ethnicity, language, and recency of immigration. Different groups may or may not communicate, cooperate, or collaborate with one another, and may compete with one another for scarce resources.

Although some well-established CBOs serve multiple racial and social groups, many focus on particular groups. In fact, many CBOs are founded by particular groups to meet the special needs of their members.

PHAs must form multiple, labor-intensive relationships with CBOs to make sure that public health initiatives in the minority community reach a broad spectrum of the individuals in need. There are few short cuts. Given the competitive forces at work in a high-need, resource-poor environment,

Table 2
Weighted prevalences of behavioral risk factors among white and minority groups, United States, 1991-1992

Indicator	White American %	African American %	American Indian/ Alaskan Native %	Asian/ Pacific Islander %	Hispanic American %
Cigarette Smoking[a]	23.0	23.0	34.3	14.8	18.1
Sedentary Lifestyle[b]	56.3	65.5	57.4	60.5	61.7
Chronic Drinking[c]	3.8	2.3	4.4	1.4	3.2
Binge Drinking[d]	15.0	9.4	17.2	8.4	16.6
Overweight[e]	23.2	33.6	32.0	10.4	25.2
High Cholesterol[f]	26.5	23.9	27.5	26.6	24.4

a - Cigarette smoking - ever smoked 100 cigarettes and currently smoke regularly
b - Sedentary lifestyle - fewer than three 20-minute sessions of leisure-time physical activity per week
c - Chronic drinking - 60 or more drinks of alcohol during the past month
d - Binge drinking - consumption of five or more alcoholic beverages on at least one occasion during the past month
e - Overweight - body mass index >= 27.8 for men and >= 27.3 for women, where BMI = kg/m^2
f - High cholesterol awareness - respondents ever told by a health professional that their cholesterol is elevated

Source: CDC, Behavioral Risk Factor Surveillance System, state aggregate data for 1991-1992

fostering cooperation among CBOs to achieve efficiencies in the deployment of public health assets is very costly, and frequently short-lived.

Inadequate Infrastructure

Most PHAs and most CBOs in the minority community have inadequate infrastructure to support effective collaborations in health promotion. Changing ingrained health risk behaviors takes years of labor-intensive effort. Doing so across cultures and languages multiplies the cost and requires special resources.

Most PHAs lack sufficient staff with the cultural competence to collaborate effectively with people from a wide variety of cultures. Typically, PHAs are organized to serve the population as a whole, not multiple subpopulations with varying needs. Recognizing this problem, some PHAs have created special organizational units to bring focus to the needs of minority populations and to coordinate minority health activities across PHA programs. Because they have done so within severe budget constraints, however, these units are very small in relation to the needs they are intended to satisfy.

CBOs in the minority community have infrastructure problems of their own. Financial resources are lacking, even in the larger CBOs. Smaller, recently founded CBOs, of which there are many, have unstable funding bases. Most derive too much of their income from grants, an unpredictable source of funding, at best. It is not uncommon for CBOs to live from grant to grant, with key staff members like the executive director providing specific services in grant-funded projects. In this context, scarce public health dollars which should go to direct services are spent on overhead, instead. Also, CBOs strapped for funding may apply for grants tangential to their central goals. At best, grants awarded in such cases are executed competently, with services ending abruptly when grant funds are exhausted. At worst, grants awarded in such cases are given short shrift by the recipient, with little impact on the communities the grants were intended to serve.

Possibilities

Surveillance is a core public health function. To maintain credibility in the minority community, PHAs must undertake effective surveillance of high-risk subpopulations, possibly by diverting assets from traditional surveillance functions. Close scrutiny of the latter may yield strategic opportunities for redeployment.

Health promotion to reduce major chronic disease risk factors may never attain the immediacy of other public health objectives among minority leaders. Nonetheless, African American leaders nationally have ranked the importance of preventing hypertension, heart disease, and stroke between *third and fourth* among 21 public health objectives, and minority leaders locally have ranked the importance of enhancing access to primary care *first* among seven high priority public health objectives. The opportunities for addressing major chronic disease risk factors (cigarette smoking, excessive fat in the diet, and insufficient physical activity) *within the context of these priorities* are obvious.

PHAs must deploy sufficient staff to cope with the racial and social diversity of the minority community. PHAs and the public at large would be well served if the racial and social diversity of PHA staff were increased through affirmative hiring practices. In today's economic climate, however, hiring opportunities of any sort are rare. As an alternative to hiring, PHAs may redeploy existing staff, training them to work effectively with people from multiple cultures in the minority community. If such staff were left in place throughout the organization to coordinate programs which bring focus to minority health, they would be positioned to recognize and develop strategic opportunities for collaboration with the minority community, and to spread multi-cultural competence to other staff members.

Having coped with their own infrastructure needs, PHAs must be very careful in coping with the infrastructure needs of CBOs in the minority community. The needs are so substantial that they may easily overwhelm the capacity of any PHA which tries to help meet them. If help is offered insensitively by

Table 3
Ranks of black leaders' opinions about the importance of health objectives for Black Americans in the U.S.

Health Objective	Health Leaders	Mayors	Legislators
Reduce alcohol and other abuse.	1	3	2
Prevent/control HIV infection and AIDS.	2	1	2
Prevent/detect/control hypertension, heart disease, and stroke.	3	4.5	4.5
Reduce violent and abusive behavior.	4	4.5	4.5
Improve maternal and infant health.	5	9	2
Prevent/control sexually transmitted diseases.	6	2	6
Prevent/detect/control cancer.	7	6	7
Reduce tobacco use.	8	13	13
Prevent/detect/control diabetes and other disabling conditions	9	7.5	8
Promote health education and community-based health programs.	10	12	10.5
Increase clinical preventive health services.	11	15.5	12
Improve nutrition.	12	10	9
Immunize against/control infectious diseases.	13	7.5	10.5
Improve mental health / prevent mental illness.	14	11	15
Increase physical activity and fitness.	15	15.5	14
Increase access to family planning services.	16	17	16
Improve environmental public health.	17	14	17
Improve oral health.	18	20	19
Improve occupational health and safety.	19	19	18
Prevent/control unintentional injuries.	20	21	21
Improve food and drug safety.	21	18	20

Source: Schneider D, Greenberg MR, Choi D. Black leaders' perceptions of the year 2000 public health goals for black Americans. AJPH 1993;83(8):1171-1173.

a PHA, the potential for collaboration with CBOs may diminish. If help is offered randomly, most of the capacity of a PHA to help build public health infrastructure in the minority community may be spent on CBOs which are so lacking in basic infrastructure that no apparent progress is made. In contrast, if PHAs and minority CBOs collaborate in a careful assessement of public health infrastructure needs in the minority community, they *may* identify strategic opportunities for building lasting infrastructure with limited resources.

Table 4
Ranks of minority leaders' opinions about the importance of health objectives for minority groups in Rhode Island

Health Objective	Rank
Enhance access to primary care.	1
Prevent domestic and gang violence.	2
Control TB and AIDS.	3
Promote healthy lifestyles.	4.5
Prevent teen pregnancy.	4.5
Control substance abuse; improve mental health.	6
Improve environmental health.	7

Good relationships between PHAs and CBOs in the minority community are so precious that considerable effort should be expended on preserving them. These inter-organizational relationships are founded on tolerance, understanding, and trust between individuals, usually representing years of personal investment. PHAs and CBOs alike must work to protect this investment, despite the endless reorganizations to which PHAs are inevitably subject. Tolerance, understanding, and trust may ultimately mean more to the public's health than the availability of tangible resources.

PHYSICIANS AS PARTNERS

PHAs would be well served by enlisting the cooperation of physicians in preventing chronic disease among minority groups. Physicians can make a difference with minority patients by reporting correct race and ethnicity data in all medical records, by communicating simple, consistent, and culturally specific prevention messages, by checking to see that patients understand important health risks, and by assuring that patients are screened appropriately for chronic diseases. If applied consistently, these activities may contribute significantly to the prevention and control of major chronic diseases.

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Health by Numbers

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

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Cancer Control Among Rhode Island's Minorities

John P. Fulton, PhD

INTRODUCTION

Rhode Island residents who are members of minority racial and ethnic groups often suffer from poor health status relative to the white, non-Hispanic population. In order to examine the differentials with respect to cancer, the Rhode Island Department of Health assessed data on cancer incidence, cancer mortality, and selected behavioral risk factors for cancer among the major racial and ethnic groups in the state's population.

METHODS

Frequencies of newly diagnosed cancers by race and ethnicity were obtained from the Rhode Island Cancer Registry for the year 1993. Cancer mortality rates were calculated from state vital records for the period 1980 - 1989 and United States Census data for 1980 and 1990. Rates were age-standardized using the 1970 population of the United States as the standard population. Tobacco use statistics were obtained from the United States Current Population Survey conducted in September 1992, January 1993, and May 1993.[1] Cancer screening data for minority women were obtained from a 1991 survey of Rhode Island women ages 40 and older residing in minority low-income census tracts. (The selected census tracts were those in the lowest quartile of a group of socioeconomic indicators and in which at least 5% of the population was Hispanic or non-Hispanic African American in the 1990 Census.) Statewide data were obtained from the Rhode Island Behavioral Risk Factor Surveillance System surveys for 1991 and 1993. Screening standards used were based on national recommendations and were as follows:

Breast cancer:

Women ages 40-49: Mammogram in past two years and clinical breast examination in past year

Women ages 50+: Mammogram in past year and clinical breast examination in past year

Cervical cancer:

Women ages 40+: Pap test in past year

[Note: Even when aggregated over several years, Rhode Island public health statistics for minority groups are usually based on few cases, e.g., few cases of cancer, few cancer deaths, and few survey respondents. Statistics based on few cases are usually associated with large standard errors and should be interpreted with due caution.]

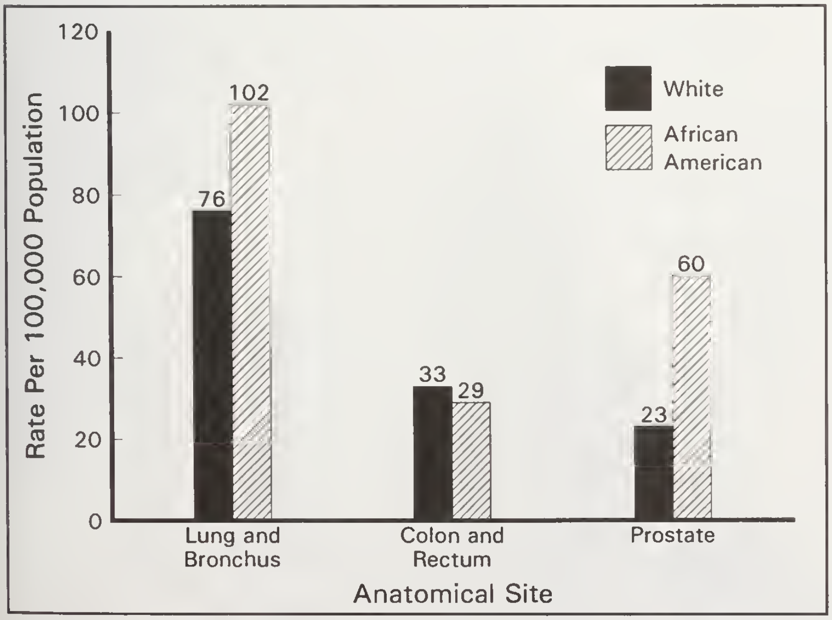

Figure 1. Age-adjusted cancer mortality per 100,000 population, males, by race, for cancers of selected anatomical sites, Rhode Island, 1980 - 1989.

Results. Of 5,486 newly diagnosed cases of cancer among Rhode Island residents in 1993, 5,172 (94.3%) occurred among non-Hispanic whites, 143 (2.6%) among non-Hispanic African Americans, 38 (0.7%) among Hispanics, and less than 1% among Asians (15), Native Americans (4), and Asian Indians (2) combined. For 112 cases (2%) race and ethnicity were not reported.

African Americans in Rhode Island, both males and females, were substantially more likely than whites to die of lung cancer during 1980 - 1989, with elevations of 34% among males and 44% among females. (Figures 1 and 2) In addition, African American men were over twice as likely as white men to die of prostate cancer. Mortality rates for cancer of the colon and rectum, female breast, and uterine cervix did not differ significantly between African Americans and whites.

Smoking prevalence in the population ages 20 and older during 1992 - 1993 was highest among African American males and lowest among Hispanic males. (Figure 3) African American men are about twice as likely to smoke as other men. Non-Hispanic African American women and His-

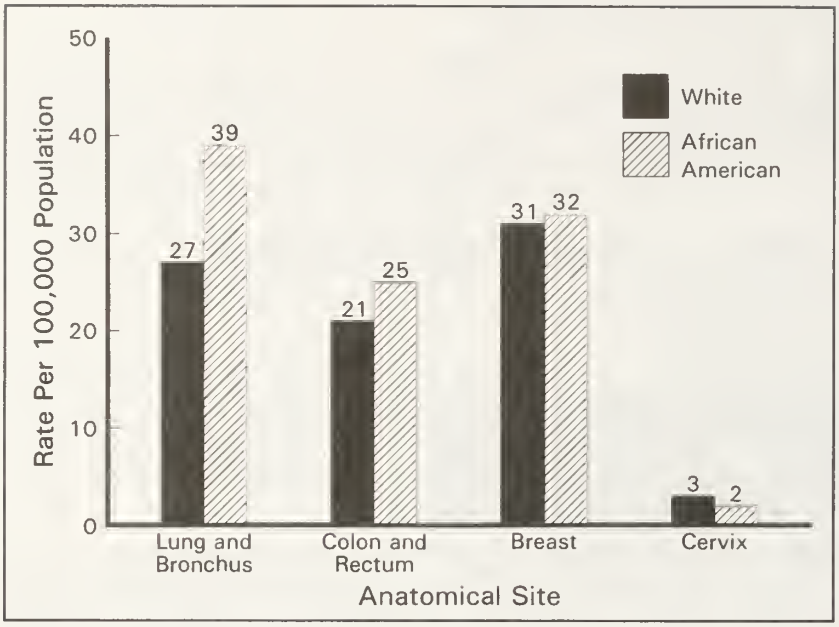

Figure 2. Age-adjusted cancer mortality per 100,000 population, females, by race, for cancers of selected anatomical sites, Rhode Island, 1980 - 1989.

panic women had about the same smoking prevalence, somewhat lower than the smoking prevalence among non-Hispanic white women.

Screening for cancers of the breast and cervix was performed less frequently among inner-city women than among women statewide in 1991. (Figure 4) Inner-city Hispanic women were half as likely as other inner-city women to have been screened for cancers of the breast and cervix according to current guidelines.

DISCUSSION

Although persons of Hispanic origin form the state's largest minority group based on race and ethnicity, there are far fewer cases of cancer diagnosed annually among Hispanics than among African Americans, the second largest minority group. This occurs in part because the incidence rates of most forms of cancer increase with age and there are fewer elderly among the state's Hispanic residents (4.5% were ages 65 and older in 1990) than among the state's African American residents (5.7% were ages 65 and older in 1990). However, much of the disparity is likely due to the under-reporting of Hispanic origin that is believed to exist in many of the state's health data sources.

Tobacco use is a major cause of cancer in Rhode Island. African American men, among whom the prevalence of tobacco use is high, experience high mortality from lung cancer, which is largely caused by cigarette smoking. Engaging the state's minority communities in tobacco control efforts is a special focus of the Department's "American Stop Smoking Intervention Study" (ASSIST).

Prostate cancer mortality is much higher among African American men than among white men in Rhode Island. This phenomenon, observed throughout the United States, is attributable to higher prostate cancer incidence and poorer access to health care among African Americans. Although the effectiveness of mass screening for cancer of the prostate is controversial, most medical authorities recommend regular use of the digital rectal examination as part of the periodic preventive health exam for men ages 40 and older. The American Cancer Society recommends annual use. Although no data exist to measure precise screening rates among African American men, Behavioral Risk Factor Surveillance System data for 1993 show that the screening rate for all men ages 40 and older was only 51% annually. It would be prudent to increase use of the digital rectal examination among African American men by increasing their access to primary care and by promoting use of the periodic preventive health exam.

Screening rates for cancers of the breast and cervix are too low among minority women in Rhode Island's inner-city areas, especially among Hispanic women, and will result in excess cancer mortality unless improved. In order to avoid this outcome, minority women have been a special focus of recent efforts to improve women's cancer screening rates in the state.

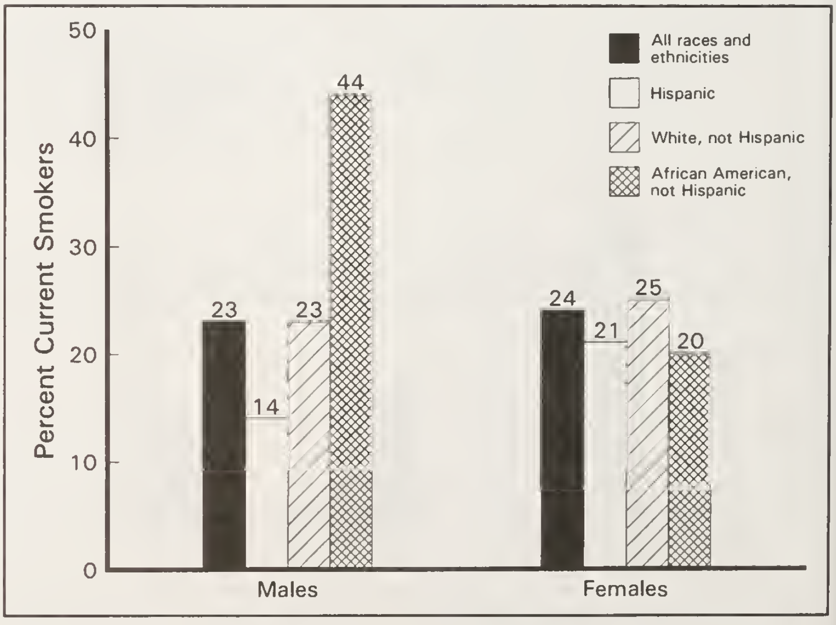

Figure 3. Prevalence of cigarette smoking among persons ages 20 and older, by race, Hispanic origin, and gender, Rhode Island, 1992 - 1993.

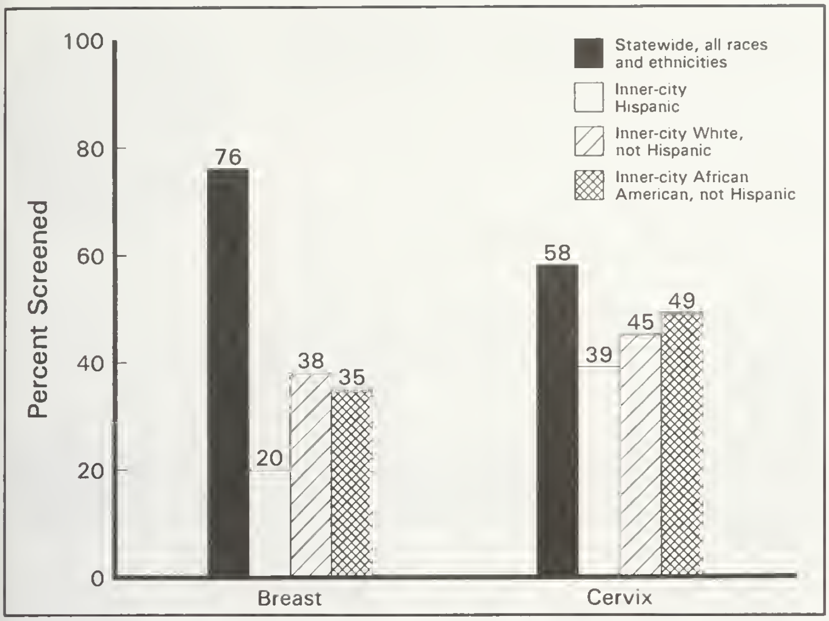

Figure 4. Compliance with screening standards for breast cancer and cervical cancer among women ages 40 and older, by location of residence, Hispanic origin, and race, Rhode Island, 1991.

REFERENCES:

1. Hartman AM. Tobacco use in Rhode Island (tables). United States Current Population Survey, Tobacco Use Supplement, Sept 1992, Jan 1993, and May 1993. Bethesda, Maryland: National Cancer Institute, 5 Oct 1994.

* * *

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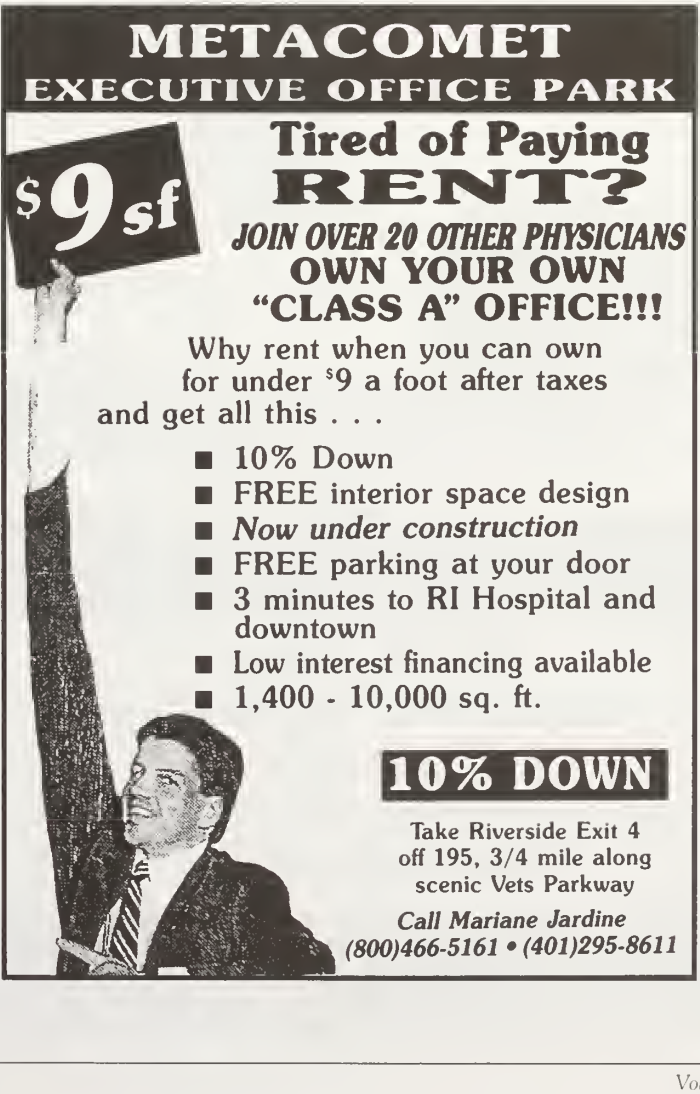
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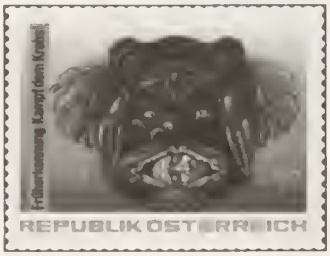
Medicine & Philately

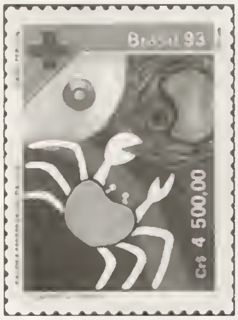
John T. Tierney

Stamp collecting is more than the accumulation of little pieces of colored paper which are viewed on occasion and then filed away. The true stamp collector puts stamps to work and uses them, hopefully, in a manner which is beneficial both to the collector and society.

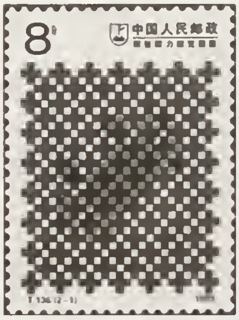
There are many ways of accomplishing this goal: One may organize stamp exhibits; or one may write articles about stamps for publication in the philatelic literature.

This author collects stamps related to health promotion and disease prevention, and publishes articles, illustrated by stamps of many nations, in several philatelic publications. Subjects that have been published include hypertension, drowning, safety belts, drunk driving, smoking, raising funds to fight cancer, breast cancer and breast feeding.

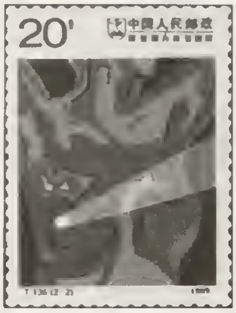




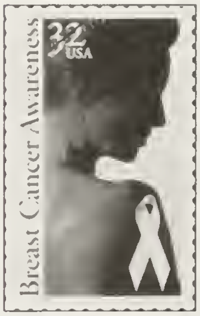
A number of nations have issed postage stamps on the subject of breast cancer. Many have used as their illustration the crab which is internationally symbolic of cancer. Note the human head in the mouth of the crab [Austria, 1976, #1043] and on the left margin the words, “Fight Against Cancer.”



Brazil [1993, #2402] depicts a Red Cross, a normal breast and one attacked by a crab. The People's Republic of China in 1989 issued #2212 which displays a grid of Red Crosses ensnaring a crab suggesting that early breast cancer detection is an effective procedure. Also part of the People's Republic of China 1989 set is #2213 with a woman undergoing diagnostic thermography [a procedure supplanted in this country by mammography.]



The United States breast cancer awareness stamp, issued on June 16, 1996, is a sensitive portrayal of a woman practicing breast self-examination. The ribbon in the lower right corner is pink and represents the symbol of breast cancer awareness. A similar ribbon which dominates the AIDS postage stamp is colored red.



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Vital Statistics

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Roberta A. Chevoya

Rhode Island Monthly Vital Statistics Report
Provisional Occurrence Data from the Division of Vital Records

Vital Events

	Reporting Period		
	Jan. 1996	12 months Ending with Jan. 1996	
	Number	Number	Rates
Live Births	843	13,501	13.6*
Deaths	841	9,730	9.8*
Infant	(6)	(96)	7.1#
Neonatal	(6)	(74)	5.5#
Marriages	222	7,402	7.4*
Divorces	260	3,659	3.7*
Induced Terminations	451	5,657	419.0#
Spontaneous Fetal Deaths	45	1,002	74.2#
Under 20 weeks gestation	(40)	(938)	69.5#
20 + weeks gestation	(5)	(64)	4.7#

* Rates per 1,000 estimated population
# Rates per 1,000 live births

Underlying Cause of Death

	Reporting Period			
	July 1995	12 Months Ending with July 1995		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	271	3,309	332.1	4,476.5
Malignant Neoplasms	223	2,436	244.5	7,041.0
Cerebrovascular Diseases	57	627	62.9	625.0
Injuries (Accident/Suicide/Homicide)	27	309	31.0	5,957.5
COPD	28	410	41.2	330.0

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.
(b) Rates per 100,000 current estimated population of 996,325.
(c) Years of Potential Life Lost (YPLL).

Note: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

THE RHODE ISLAND MEDICAL JOURNAL

The Official Organ of the Rhode Island Medical Society
Issued Monthly under the direction of the Publication Committee

VOLUME 1
NUMBER 1

PROVIDENCE, R.I., JANUARY, 1917

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NINETY YEARS AGO

JULY, 1906

The lead editorial, entitled Clean Milk for Babies, decries the high yearly infant mortality rate arising particularly during the summer months and is ascribable to contaminated milk and food supplies. The editorial points to various effective programs both overseas and in in the United States where sterilization of the milk supply, often by a process called Pasteurization, has virtually eliminated this tragic rise in infant mortality. In response to this public health problem, a number of Providence physicians have convened to develop a plan to provide a safer milk supply for the local infants and children. The plan envisages five milk stations scattered through Providence, each offering clean milk in bottles for prices of one to two cents per bottle. The quality and purity of the milk will continue to be under the surveillance of the Department of Health. "This plan cannot succeed unless it meets with the approval, and secures the cooperation of the physicians of the city." The editorial estimates that $1,500 will need to be raised to meet the anticipated expenses.

Christopher F. Barker, MD, in an address before the Rhode Island Medical Society, ponders the nature and dimensions of the physician's obligation to his profession, his colleagues and his patients. One of these obligations, he contends, rests in insuring that the educational curriculum and the educational standards needed for the future physician be the highest in the world. "Many of us can remember when the best medical schools in this country required of matriculants only a grammar school education, and conferred a degree after the completion of three courses of lectures - each covering a period of about five months, and if the matriculant was a college graduate he was required to take only two such courses. In these courses no clinical work was done by the student; the only clinical instruction afforded was given in the amphitheater where demonstrations by instructors were made before the class. The same was true of laboratory work in chemistry and physiology. Bacteriology was then in its infancy and the microscope was an unfamiliar instrument." The speaker then dwells upon the recent drive, particularly by The American Medical Association, to raise the medical school admission standards, to lengthen the required course of study and to establish guidelines for uniform licensure examinations throughout the States. He then discusses the physician's obligation to his professional associates in terms of etiquette and tolerance. Finally, he talks of the greatest of the physicians' obligations - to his patients - through commitment, devotion, solicitude, gentleness and sincere friendship.

FIFTY YEARS AGO

JULY, 1946

The lead article is written by George Blumer, MD, on the subject of the virus type of infectious hepatitis. Some 23 years before, the author had previously summarized the available knowledge in this field. At that time he emphasized the following important characteristics of the disorder: Its close association with warfare; its distinction from spirochetal jaundice; that the ordinary catarrhal form of jaundice was the sporadic form; and that it bore some relationship to acute yellow atrophy of the liver. On the basis of over two decades of further experience as well as the many inquiries into the pathogenesis of infectious hepatitis undertaken during World War II, he now concludes: The common form of infectious hepatitis in the U.S. is almost certainly due to a virus. In addition to the spontaneously occurring disease, these is a clinical indistinguishable type transmitted by vaccines containing human blood, convalescent sera or by whole blood. Catarrhal jaundice is probably the same disease as infectious hepatitis. There is no clear dividing line between the hepatic lesions of hepatitis and acute necrosis of the liver. Further, it seems that liver damage persists long after clinical recovery. He concludes: "In addition to complete rest and a long period of convalescence the essentials of treatment consist of a high carbohydrate and adequate protein intake, the avoidance of fats during the icteric stage and, especially in the more serious cases, the use of methionine which protect liver cells."

Eric Denhoff, MD describes cerebral palsy, not as one disease but as a variety of syndromes with varying degrees and forms of neuromuscular dysfunction. Specific symptoms may include spasticity, athetosis, ataxia, rigidity and tremors, singly or in combination. The author notes: "Functional self-sufficiency is the aim of any re-educational program. Physical therapy, utilizing relaxation, is the basis of good treatment. Curare and neostigmine, as adjuncts to physiotherapy promise to be of value in cerebral palsy."

Lt. Walter T. Zimdahl, MC provides a preliminary report on employment of the Crawford Allen Hospital - a division of Rhode Island Hospital - for the diagnosis and care of children with rheumatric disorders.

An article, written by the Director of the National Farm Bureau details the medical needs of the rural communities of the United States.

Twenty-Five Years Ago

July, 1971

Eugene A. Stead, Jr, MD gives the Thirtieth Charles V. Chapin Oration describing a training program for the preparation of tomorrow's generalist. His innovative proposal considers first the selection of students, noting that a separate admissions committee in philosophic agreement with the objectives of the program is essential. Selection criteria should emphasize synthetic rather than analytic abilities, interest in primary care as a career and experience with such office sites as rural communities or inner cities. Before beginning formal medical school, the student will spend several months in the office of a generalist. Year One curriculum will introduce the student to the language of medicine, to topographic anatomy, to interviewing technics, epidemiology and the basic sciences. Clinic work will be interspersed with classroom exercises. In Year Two, the student will be assigned to the clinical wards, intentionally mixing patients from the various types of services; the base will be a community rather than a university hospital. Year Three will expose the student to management, records and the general rudiments of general practice. Some basic sciences and specialty training in such disciplines as gynecology, ENT and dermatology will be provided. Year Four will be invested in family practice clerkships. Following graduation the physician will be assigned to the office of a family practitioner. The author concludes: "Adventures of this type will not be successfully tried by schools long established and fixed in their ways. They could never gain approval of the faculty. They cannot be mounted by new schools because both the faculty and students have to prove themselves by jumping all the usual hurdles. They can be tried by strong schools in mid-course who have the tradition of producing excellent clinicians."

Robert J. DeLorenzo, winner of the Fiske Fund prize essay, describes how isozymic variants are used as genetic markers for clarifying the genetic control, expression, linkage and chromosomal mapping of specific enzyme loci in normal and diseased populations.

Dr. Ian Macnab, offering the Thirteenth Murray S. Danforth Oration, discusses the painful shoulder caused by rotator cuff tendinitis. "This form of tendinitis presents as a series of symptom complexes, depending on whether the lesion is local or diffuse. These symptom complexes are readily identified, and each demands a specific type of therapy. Although this is an oversimplification of an ill-understood problem, it is hoped that by presenting it in this manner it will be possible to direct treatment along rational lines."

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Illustrations and charts must be submitted in black ink on white paper. Laser-printed graphs are acceptable, provided they are printed at 300 DPI resolution.

Photographs must be in black and white, submitted on 5" x 7" glossy paper.

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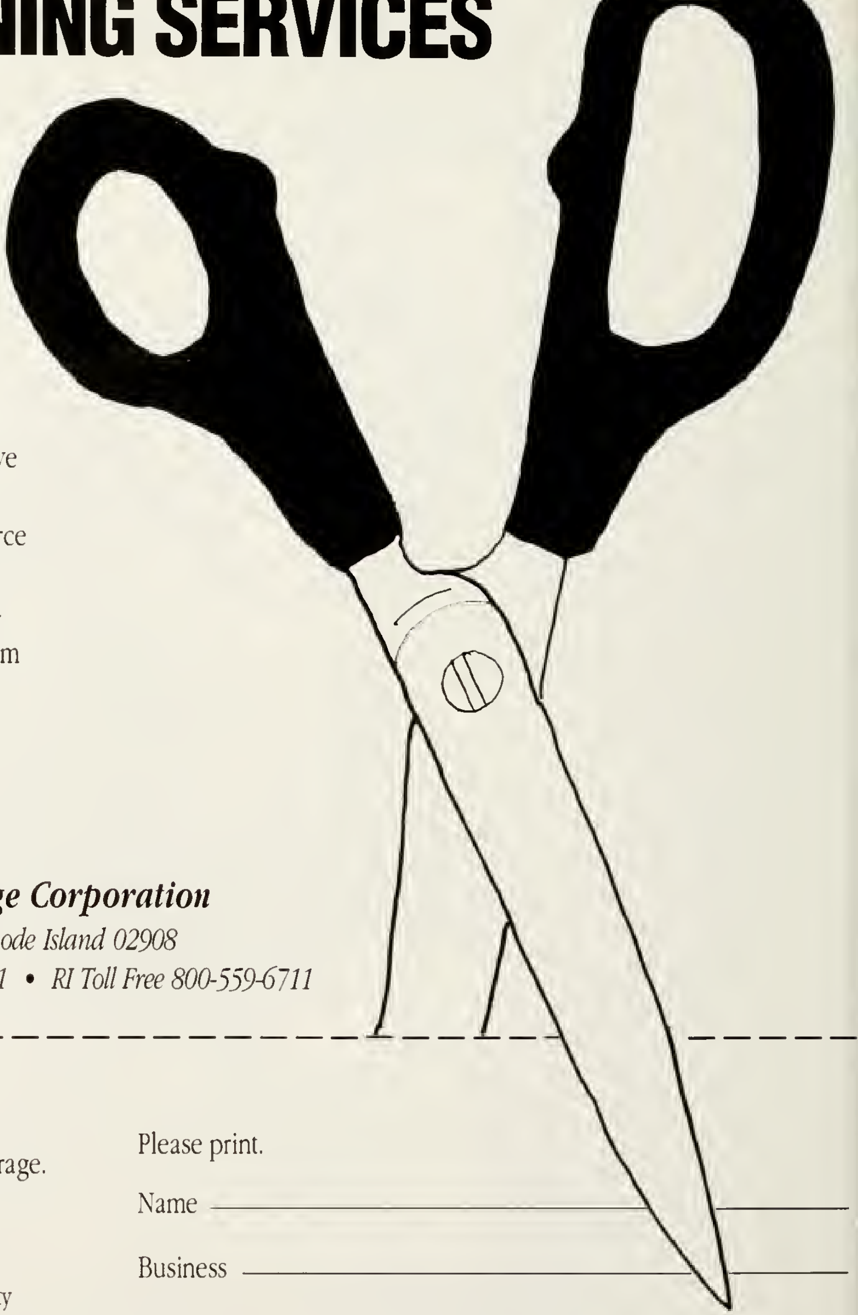

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COMMENTARIES

The Mother of All Universities

On May 27 of this year Brown proudly awarded the degree of doctor of medicine to 88 men and women who had matriculated at the University and who had fulfilled all of their alma mater's stated academic requirements. A diploma has been bestowed on each graduate signifying their doctoral status and making them alumni and alumnae of this University. This issue of *Medicine & Health/Rhode Island* , under the guest editorship of Stephen R. Smith, MD, lists these new colleagues, defines their intended specialties and specifies the locations of their residency training programs.

The preceding paragraph is liberally sprinkled with certain operative words which expressively convey the traditional yet joyous spirit of this occasion. Words such as university, alma mater and academic clearly relate in some manner to an institution of higher learning; while words such as matriculation, graduation, alumni, diploma and degree serve to define the act of departure as well as provide tangible recognition of a scholarly task fulfilled. The historic rituals and solemnity of the event move one to believe that these words have always pertained largely, if not solely, to the ancient trappings of higher education.

But, far from being eternally wedded to the cloistered world of academia, most of these words, in fact, bear a distinctly maternal rather than collegial air. Alma mater, in Latin, means nourishing or bountiful mother. The phrase was first used by the Romans to describe their Earth-mother goddesses Cybele and Ceres and only belatedly referred to universities. Alma descends from the Latin *alere* meaning to nourish [and is thus related to such words as alimentary and even alimony.] On a deeper level, it is cognate to the Hebrew *alma,* meaning young woman. The words alumnus and alumna, representing the male and female graduates of an institution of learning, also derive from the Latin *alere,* but originally designated a foster child. The metaphoric sense of an adopted offspring of a university was only employed in the 18th century. Matriculate, from the Latin *matriculare* means to register or to enroll; it was first used to describe the permanent recording of a legislator's or soldier's name upon some official rosters. It conveyed, somehow, the sense of adoption by - and allegiance to - a new institution but without the slightest hint of campus life. The word eventually traces its origin to the Greek *matra* meaning womb [see such words as matrimony, endometrium and metralgia]. The Greek mother city from which subsequent satellite communities had arisen was therefore called metropolis.

The word, graduate, descends from the Latin *gradus* meaning a step or a degree of change. And from this same root came such current English words as gradation, gradual, congress, egress, degrade - and degree. Degree is derived directly from the Latin *degradus* meaning, unambiguously, a step down. A now obsolete meaning then defined a degree more neutrally as one of a flight of stairs, either up or down, or merely a single step in a continuing process leading to some specified endpoint. Only recently has the word been used to describe the attainment of a particular level of skill or competence [as in college degree.] When used in an academic context, a degree is therefore an ascending step only. But when used forensically, it conveys a more somber tone suggesting intensity rather than direction [as in first degree murder; second degree burns; or third degree interrogation.]

The word, university, comes from the Latin *universitas,* describing a population of persons with a unified purpose congregating in a body. The meaning has narrowed now to describe more the physical plant rather than its contained population. The word, varsity represents a contraction of university. And academe was the name of the Attic forest in which Plato enlightened his many students [" . . . and seek for truth in the groves of Academe."]

The word, diploma, is derived from the Greek *diplos,* meaning a doubled or folded document as in ancient commercial contracts. It later came to describe state papers [and those who carried such documents were thus called diplomats; their art of tactful dissembling and deceptive negotiating came later.] Only in recent centuries has the word been appropriated to define a document, issued by a competent academic authority, attesting to the completion of some scholarly task.

The rite of graduation, this past May, was indeed a memorable occasion: for the new graduates; for their family and friends; and, vicariously, for the large numbers of Rhode Island practicing physicians who had participated actively in the clinical education of their new colleagues. This was truly a unique occasion; and the magisterial words which define this rite of passage are equally special. Some boast of an uncluttered path back to their semantic roots in one or another classical tongue. Others have strayed significantly from their original intent, with numerous changes - or at least gradations - in meaning. But none of these words [defined long before colleges had ever been established] bore any initial relationship to scholarly activity until recent centuries. Most of these grand ceremonial words, in truth, are traced back to ancient words imparting a feeling of maternal embrace and support, perhaps reflecting the early historic realities of higher education as a transition to a new life where the monastery school replaced the mother - *in loco parentis* - as a source of sustenance, guidance and education.

Does a knowledge of the life history, the etymological pilgrimage, of these glorious words really make the awarding of the MD degree more meaningful? Probably not. And will this semantic information, in any fashion, aid this cohort of new physicians overcome the countless clinical dilemmas that will soon encounter? Clearly not. But medicine has always encouraged its practitioners to look beyond surface appearances; to weigh with discrimination the subtle nuances which disguise the elements in any complex picture making each appear other than what they really are; to seek out contributing factors, causes, even origins; to determine the seats as well as the faces of disease. A compelling sense of curiosity, learned through years of rigorous education, will inevitably spill over into pursuits unrelated to disease; and the compulsion to overcome the tyranny of ignorance, therefore, continues to be an abiding attribute of most physicians. It is not an odd coincidence that Rabelais, Keats, Conan Doyle, Chekhov, Maugham - and even Michael Crichton - were all first trained as physicians.

Stanley M. Aronson, MD

Ode to the Mosquito

Summer is here; and with it comes such naturally ordained events as warm breezes, blossoming perennials - and the proliferation of insects. So, the next time that you swat a mosquito [the *Culidae*] it would be well to contemplate the lineage and malevolent majesty of this frail creature. Paleontologists tell us that they have been buzzing around, essentially unchanged, for about 120 million years - a substantially longer interval than the hominid reign of but 3.6 million years. Fossils mosquitoes have been found in Cretaceous strata well before mammals had evolved giving rise to speculation that they had fed originally on birds, amphibians and reptiles.

Those who look at the larger picture say that the sole purpose of the fly swatter is to give the wielder some slim avenue to vent his frustration. But destroying one or ten - or even a thousand - mosquitoes by physical impact, while ecologically sound, changes the total dynamics of mosquito populations little except to prompt an increased fecundity by the survivors since mosquito density is determined, not by fly-swatter efficiency, but ultimately by available breeding and feeding sites. Thus, killing mosquitoes without compromising their places of procreation does little to diminish their effective numbers. It is akin to undertaking rain forest defoliation by plucking leaves, one at a time.

Were we to measure the mass of all living creatures - vertebrate and invertebrate, huge and small - insects would comprise fully 80% of the total biomass of this globe. And while insecticides and sanitary engineering interventions have exerted some temporary restraints on insect density in small regions, for finite intervals of time, the total numbers of insects [including those which are vectors of major diseases] are as great today as have ever prevailed before the true evil wrought by insects, particularly mosquitoes, was recognized in the late 19th century.

Gender differences in the morphology of the antennae and proboscis, amongst the *Culidae*, are readily apparent to the trained entomologist, and presumably also to mosquitoes of the alternate sex. These structural differences reflect a striking divergence in their sources of nutrition. While both sexes rely heavily on feedings from sugared fluids such as nectars, the female alone will require mammalian blood feedings which she uses as her sole source of protein for the maturation of her eggs. The average amount of blood extracted by the female, per bite, is 4 mg.

The mosquitoes, with some 3,450 species, have achieved a global distribution sparing only the Antarctic and a few isolated Pacific islands. They have been troublesome irritants to man for millennia making certain regions, particularly in west Africa, virtually uninhabitable. The particulars of their true villainy, however, dates to the 1877 paper by Patrick Manson demonstrating the role of the mosquito as the biologic vector of Bancroftian filariasis. Within the next five decades these frail insects were shown to be the sole carriers of malaria and a variety of viral diseases including yellow fever, dengue and most of the arthropod-borne encephalidites such as equine encephalitis.

Five major genera of the *Culidae* [*Anopheles, Aedes, Culex, Mansonia* and *Haemagogus*] account for most of the mosquito-borne diseases. Some of the names given to the mosquitoes are rather neutral, describing physical attributes such as color or body structure. Most of the names, however, reflect the profound respect they engender in medical entomologists. The name, mosquito, represents the Spanish diminutive of the Latin *musca*, meaning fly. *Anopheles* [Greek *an-* meaning without; and *ophelos*, meaning gain; ie, useless or harmful] comprise some 422 species at least 70 of which are active carriers of malaria. Anopheline species may also carry other diseases such as filariasis. *Aedes* [Greek, *a-* meaning without; and *edus*, meaning sweet; ie, distasteful] species are the principal carriers of yellow fever and dengue. *Culex* [Latin, *culex*, meaning gnat or small insect] species are vectors for *W. bancrofti* filariasis. *Mansonia* [honoring Patrick Manson] and *Haemogoga* [Greek, meaning gatherer of blood] are also vectors for yellow fever.

Some of the Anopheline species names mirror the havoc they have wrought. *A. funestus* [Latin, *funus*, a burial, as in the word funeral]; *A. atroparvus* [Latin, *atrox* meaning barbarous; and *parvus*, meaning puny]; *A. cinereus* [Latin, *cinereus* meaning the color of ashes, as in the word incinerate]; *A. aconitus* [Greek, *a-* meaning without; and *koniein*, meaning dust; ie, unconquerable. Aconite is also the name of a family of poisonous plants, such as monkshood. The Greek word *koniein* is cognate with the Latin *cinereus* - see above.] Other species names are of geographic purpose [eg, *A. gambiae*, *A. arabiensis*, etc.]. Yet others describe their ecologic niche [*A. fluviatilis*, Latin, *fluvius* meaning river.]; *A. campestris* [Latin, *campester*, meaning a flat field as in the word campus.] And still others take note of some anatomical feature [eg, *A. annulifera;* Latin, *anulus* meaning ring; and *ferre* meaning to carry; *A. quinquefasciatus;* Latin, *quinque* - meaning five; and *fascia,* meaning a bundle or a band.

A 17th century poet declared: ". . . every particle of an insect carries with it the impress of its Maker and can read us lectures on ethics and divinity." Perhaps so. But it is well to point out that this rhapsodic proclaimer of the divine nature of each bug lived his life in northern Europe, far removed from the perils of yellow fever or malaria or dengue. The mosquitoes, unpoetical epidemiologists now assert, have slaughtered more humans in recent centuries than any swarm of tyrants.

Stanley M. Aronson, MD

The Mark of a Scientist

Scotland's preeminent ophthalmologist, Douglas M.C.L. Argyll Robertson [1837 - 1909], established an honored place for himself in neuro-ophthalmologic history by describing, in patients with tabes dorsalis, abnormal ocular pupils which react to accommodation but not to light. His fame widened when he was chosen as Queen Victoria's surgeon-oculist. But his most signal contribution to humanity derives from his investigations, at age 26, into the toxic alkaloids contained within the Calabar bean.

> For more than a year past I have recognized the numerous advantages that would flow from the discovery of a substance which, when applied to the conjunctiva, should produce effects exactly opposite to those well known to result from belladonna or atropine; which should stimulate the muscle of accommodation and the sphincter pupillae as the above-named remedies paralyze them.[1]

Robertson prepared a weak extract of the Calabar bean which he then instilled upon the conjunctiva of his own left eye. At 20 minute intervals he then measured the diameters of his pupils, noting first that the drug produces a temporary shortsightedness and second that "it occasions contraction of the pupil and sympathetically, dilatation of the pupil of the other eye." His further experiments affirmed that the extract did indeed antagonize the mydriatic effects of atropine.

The Calabar bean, named after a west African port in southern Nigeria, is a leguminous plant which attains heights of over 50 foot. Its seed pods contain two to three chocolate-colored beans which are rapidly poisonous if ingested whole. Pod extracts, in very small amounts, have been used by local populations to embellish certain religious ceremonies. Locally, the plant was called the Ordeal Bean because it was regularly administered to those brought to trial under suspicion of witchcraft; if the suspect survived the ordeal [similar to colonial New England's infallible water assays for witchhood] she was deemed innocent. Larger doses of the Calabar extract regularly causes increased salivation, sweating, intense vomiting, diarrhea, bradycardia and, inevitably, respiratory arrest and death. The antidote for this intoxication is atropine.

The Calabar plant bears the technical name Physostigma venonosa and its active alkaloids are calabrine and physostigmine [eserine.] Since 1876 physostigmine, in solutions between 0.25 and 1.0 %, has been regularly employed as a topical conjunctival agent in the treatment of glaucoma. It is a miotic drug which inhibits local cholinesterase and hence, amongst other properties, results in a lowered intraocular pressure. Other agents which lower pressure in glaucoma include the beta-blockers, carbonic anhydrase inhibitors and certain sympathomimetic drugs.

The name, physostigmine [from the Greek *physo-* meaning inflated; and *stigma,* meaning a brand or a puncture] describes the unusually ballooned profile of the Calabar flower and its distended stigma, that terminal portion of the pistil which receives the pollen. The species name, *venonosa* , drew attention to its toxic properties.

The word, stigma, has meant many things. Its original connotation was narrow, describing a skin puncture or a brand [such as the tattoo identifying a Grecian slave]. It later came to mean a reproach or a sign of infamy as in the mark of Cain [Gen. 4:15]. Stigmata might therefore represent a societal censure [such as a scarlet letter or the phrase, stigma of illegitimacy], or alternatively tangible proof of some vile disease [the stigma of leprosy.] By the late 19th century, physicians also talked about the stigmata of the morphinist [ie, needle marks in narcotics addicts] or the vascular stigmata on the face of the chronic alcoholic. With some who were deeply religious, the word assumed yet another meaning: it became a sign of duress, sacrifice or martyrdom. When Francis of Assisi died in 1226 he bore visible signs - stigmata - similar to the wounds of Christ. The appearance of skin stigmata on those defending their faith, as with St. Catherine of Sienna, was taken by many as evidence of singular devotion. The Vatican, on the other hand, has expressed deep skepticism that such wounds are divinely created. To the zoologist, unmoved by either social or theologic interpretations, a stigma is the name given to the respiratory pores of the insect; and to the botanist, it is the receptive segment of the female pistil. [The male organ of a flower is called the stamen because of its resemblance to a thread [Latin, *stamen,* meaning thread]. In fabric generated by a loom, the lengthwise thread [the warp] is also called the stamen. The metaphor of the fateful threads of life led to the adoption of stamen in its plural form - stamina - as a measure of one's tenacity in clinging to life.]

The root, stigma, enters into a number of words. Stigmatism describes the physical property of a lens to focus rays of light with precision upon a single point. The inability of the human lens to focus sharply upon the retina, therefore, bears the diagnostic name of astigmatism - which finally brings us back to the realm of Argyll Robertson's ophthalmology.

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Stanley M. Aronson, MD

The Brown University School of Medicine Class of 1996

Stephen R. Smith, MD

On May 27, 1996, 88 men and women received the Doctor of Medicine degree from Brown University representing the 22nd class of physicians graduated from that institution in this century. If this class follows the pattern of preceding classes, approximately 14% will eventually enter the practice of medicine in the State of Rhode Island. Of the 1,486 physician graduates of previous classes, approximately 213 (14%) are currently licensed to practice in Rhode Island.

The purpose of this article is to introduce the graduates of the M.D. Class of 1996 to the physician community in Rhode Island, since many will be your future professional colleagues.

A Portrait of the Class of '96

Forty-seven graduates were men (53%) and 41 were women (47%). The racial/ethnic composition of the class, as shown in Table 1, is similar to the previous year in the proportion of students from Asian-American backgrounds (28%). About half of the students in the first four undergraduate years of the eight-year Program in Liberal Medical Education (PLME) are Asian American. Only 5% of the graduates are members of minority groups underrepresented in medicine (4 African Americans) as defined by the Association of American Medical Colleges (AAMC). Two other graduates are Hispanics. This number is disappointingly low, but should rise in future years based on more successful recruiting of underrepresented minority students in the PLME. For the past four years, about 20% of freshmen college PLME students have been from underrepresented minority groups. The percentage of underrepresented minority students in the first three years of the medical school is 12.2%.

Abbreviations Used

AAMC	Association of American Medical Colleges
EIP	Early Identification Program
PLME	Program in Liberal Medical Education

Slightly more than one fifth of the class (18 graduates) are residents of Rhode Island. The Rhode Island students in this year's graduating class came from 11 different communities in the state, with 7 from Providence, two from West Warwick, and one each from Barrington, Cumberland, East Providence, Esmond, Lincoln, North Kingstown, Portsmouth, Tiverton, and Woonsocket. The high schools from which the students graduated generally reflects this diversity, with two students each having attended Classical and Portsmouth Abbey, and the rest having come from 14 other high schools.

The number and proportion of the class going into family medicine was higher than it has ever been.

The M.D. Class of 1996 reflects the growing proportion of students from the PLME, with 36 such graduates (41%) having come through that route. The second largest cohort of students (27 graduates) came through the combined Brown–Dartmouth Medical Education Program in which students spend their first two years of medical school at Dartmouth, then transfer to Brown for the final two years.

The medical school entered into special agreements with several postbaccalaureate premedical programs (Brown University, Bryn Mawr College, and Columbia University) shortly after the PLME was inaugurated. Students from these programs decided upon a career in medicine only after completing college. Typically, they had been engaged in other careers for several years following college. The goals in establishing this new route of admission were to maintain a rich diversity in the student body by admitting students who were older and who had different academic and life experiences as well as rounding out the total class size to compensate for the expected attrition from the PLME.

Postbaccalaureate students represented 16% of the graduates. Of the 14 postbaccalaureate students, 10 came through Bryn Mawr College, 3 from Brown, and 1 from Columbia University.

Among the remainder of the class, three students were part of the Early Identification Program (EIP), two from Providence College and one from Rhode Island College. EIP students are offered provisional admission to the medical school during their sophomore year at their respective undergraduate colleges. Of the remaining graduates, two were in the MD/PhD program, one was an advanced transfer student, and the other five were through regular admissions, an avenue no longer available.

Brown University was the most common undergraduate college among the graduates accounting for 45 graduates (51%). Dartmouth College ranked second with five members of the Class of 1996, and the University of Pennsylvania third with 3 graduates having that school as their alma mater. Altogether, the graduates of the Class of 1996 came from 29 different colleges and universities.

The most common undergraduate major among the class members was biology (including subdisciplines such as plant ecology, neural sciences, microbiology), with 42% the class selecting that as their undergraduate field of study. Science majors taken together (including psychology) accounted for 59% of all majors, while 20% majored in the humanities and 21% majored in the social sciences. Among the humanities majors, history was the most common choice, while economics was the most popular choice among those majoring in the social sciences. The selection of major among the graduates represents a continuing trend toward a broader

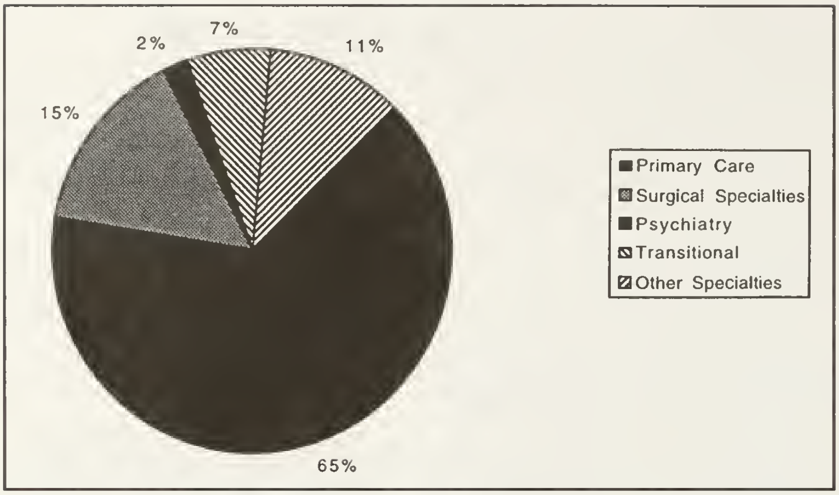

Figure 1. Specialty Choices of the Brown University School of Medicine Class of 1996

range of undergraduate majors, reflecting the larger proportion of postbaccalaureate and PLME students in this class. The postbaccalaureate and PLME students were less likely to be science majors than were traditional premedical students.

WHERE THEY ARE GOING

Internal medicine remains the most frequently selected specialty. The proportion of the graduates entering internal medicine is slightly higher than last year. The proportion of graduates choosing internal medicine seems to have plateaued in the range of 25% to 30%, as shown in Table 2.

The proportion of the class entering specialties in primary care jumped to nearly two thirds of the class (65%). This includes the fields of internal medicine, pediatrics, family practice, and obstetrics and gynecology. The number and proportion of the class going into family medicine was higher than it has ever been. Figure 1 illustrates the specialty choices of the Class of 1996.

The actual number of graduates who will eventually practice primary care after completing their graduate medical education training will be smaller than the 65% reported here, if the past is any indication. An analysis of longitudinal data collected by the AAMC of the graduates of the classes of 1987–1991 reveals that over half of the graduates who enter residency programs in internal medicine end up in a subspecialty of internal medicine, such as cardiology. Likewise, about a quarter of those entering residency training in pediatrics will do likewise.

The data for Brown graduates is similar to the national AAMC longitudinal study data. Of those Brown graduates in the MD classes of 1987–1991, only 46% of those entering residencies in internal medicine actually went into general internal medicine practice. In pediatrics, the figure is 59%. Among the primary care residencies, only family practice does not exhibit this pattern. Actually, the number of graduates in those five classes who eventually enter family practice is greater than those who started out that way by about 14%. The AAMC data is not very informative about subspecialization in obstetrics and gynecology. The Brown data shows that 96% stay in the field of obstetrics and gynecology, but the proportion who subspecialize is not known.

Applying this data to this class, about 37 graduates (42%) will actually practice in primary care. The changing climate in health care delivery is likely to increase that number, as graduates recognize that job opportunities in subspecialty medicine become harder to find.

A similar trend is seen at the national level. For the second year in a row, more than 50% of U.S. medical school seniors will pursue training in internal medicine, pediatrics, and family prac-

Table 1
DEMOGRAPHIC CHARACTERISTICS OF THE M.D. GRADUATES OF THE BROWN UNIVERSITY SCHOOL OF MEDICINE CLASS OF 1996

	No.	Percent
SEX		
Male	47	53.4
Female	41	46.6
RACE		
White	57	64.8
Asian	25	28.4
African American	4	4.5
Hispanic	2	2.3
STATE OF RESIDENCE		
New York	19	21.6
Rhode Island	18	20.5
California	10	11.4
New Jersey	9	10.2
Florida	5	5.7
Massachusetts	4	4.5
Connecticut	3	3.4
Illinois	2	2.3
Michigan	2	2.3
Pennsylvania	2	2.3
Washington	2	2.3
Other States	11	12.5
Other Countries	1	1.1

Table 2
SPECIALTY CHOICES OF THE M.D. GRADUATES OF THE BROWN UNIVERSITY SCHOOL OF MEDICINE CLASSES OF 1992-96

	Graduating Class									
	1992		1993		1994		1995		1996	
Specialty Choice	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Primary Care, total	49	(64.5)	39	(54.2)	44	(58.7)	41	(58.6)	53	(64.6)
Internal Medicine, total	22	(28.9)	20	(27.8)	23	(30.7)	18	(25.7)	25	(30.5)
Categorial Medicine	16	(21.1)	16	(22.2)	20	(26.7)	15	(21.4)	18	(22.0)
Primary Care Medicine	6	(7.9)	4	(5.6)	3	(4.0)	3	(4.3)	7	(8.5)
Pediatrics	11	(14.5)	4	(5.6)	10	(13.3)	14	(20.0)	10	(12.2)
Family Medicine	10	(13.2)	9	(12.5)	6	(8.0)	4	(5.7)	13	(15.9)
Medicine-Pediatrics	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.2)
Obstetrics & Gynecology	6	(7.9)	6	(8.3)	5	(6.7)	5	(7.1)	4	(4.9)
Surgery	2	(2.6)	2	(2.8)	7	(.93)	7	(10.0)	4	(4.9)
Surgical Subspecialties, total	9	(11.8)	10	(13.9)	8	(10.7)	9	(12.9)	8	(9.8)
Ophthalmology	6	(7.9)	2	(2.8)	2	(2.7)	3	(4.3)	2	(2.4)
Orthopedics	1	(1.3)	3	(4.2)	4	(5.3)	3	(4.3)	4	(4.9)
Neurosurgery	1	(1.3)	1	(1.4)	0	(0.0)	0	(0.0)	0	(0.0)
Urology	0	(0.0)	2	(2.8)	1	(1.3)	3	(4.3)	0	(0.0)
Plastic Surgery	0	(0.0)	1	(1.4)	0	(0.0)	0	(0.0)	1	(1.2)
Otorhinolaryngology	1	(1.3)	1	(1.4)	1	(1.3)	0	(0.0)	1	(1.2)
Emergency Medicine	3	(3.9)	2	(2.8)	1	(1.3)	0	(0.0)	3	(3.7)
Psychiatry	4	(5.3)	3	(4.2)	7	(9.3)	3	(4.3)	2	(2.4)
Neurology	3	(3.9)	3	(4.2)	1	(1.3)	2	(2.9)	4	(4.9)
Transitional & Preliminary	1	(1.3)	8	(11.1)	3	(4.0)	0	(0.0)	6	(7.3)
Institutional Specialties, total	5	(6.6)	5	(6.9)	4	(5.3)	8	(11.4)	2	(2.4)
Anesthesiology	1	(1.3)	2	(2.8)	0	(0.0)	3	(4.3)	0	(0.0)
Pathology	2	(2.6)	1	(1.4)	0	(0.0)	0	(0.0)	1	(1.2)
Rehabilitation Medicine	1	(1.3)	1	(1.4)	1	(1.3)	1	(1.4)	1	(1.2)
Radiology & Radiation Oncology	1	(1.3)	1	(1.4)	3	(4.0)	4	(5.7)	0	(0.0)
TOTALS*	76	(99.8)	72	(100.0)	75	(99.9)	70	(100.1)	82	(100.0)

*Excludes those not entering residency training in the same year of graduation. Totals do not add to 100.0 due to rounding.

tice, according to the AAMC.[1] (The AAMC does not include obstetrics and gynecology among the primary care specialties.) The number of U.S. medical school seniors who will pursue training in family practice now totals 2,276, a 9.4% increase over last year. They constitute 17% of all matched U.S. seniors.

U.S. seniors entering first-year internal medicine residencies will number 3,419, a 2.9% increase from the prior year. In pediatrics, the numbers are 1,593 and 6.1% increase respectively.

Table 4 lists the Class of 1996 graduates and where they will be going to do their residency training. Of the 82 graduates who will enter residency training next year (six are delaying their residencies for one or more years), 12 graduates (15%) matched with Brown-affiliated residency programs and will be staying in the state. Boston also attracted a dozen members of the Class of 1996 for their first year of training. This graduating class displayed a previously unseen preference for Rochester, Minnesota, with six graduates going to the Mayo Graduate School of Medicine, tying New York City and vicinity for third place.

Massachusetts will be the homes for 16 graduates next year and exceeds Rhode Island as the most popular state for residency training. Table 3 lists those states where the graduates will be going for their first year of residency training. Departing from the geographical preferences seen with preceding classes, over a quarter of this class will be locating in the South and Central states. The percentage staying in the Northeast is down slightly from previous classes (61% versus 65%), but the proportion going to the West Coast is down sharply (13% versus 25%).

CONCLUSION

The pattern of career choice of the M.D. Class of 1996 reflects the national trend toward careers in primary care and away from subspecialties. The decline in popularity in the West Coast may reflect an awareness of the job scarcity for physicians in that part of the country, but

Table 3
STATE IN WHICH THE FIRST YEAR OF RESIDENCY TRAINING IS LOCATED FOR THE BROWN UNIVERSITY SCHOOL OF MEDICINE M.D. CLASS OF 1996

State	No.	Percent
California	7	(8.5)
Connecticut	5	(6.1)
District of Columbia	2	(2.4)
Illinois	7	(8.5)
Maine	1	(1.2)
Massachusetts	16	(19.5)
Michigan	1	(1.2)
Minnesota	6	(7.3)
Missouri	2	(2.4)
New Mexico	2	(2.4)
New York	9	(11.0)
Pennsylvania	5	(6.1)
Rhode Island	12	(14.6)
South Carolina	1	(1.2)
Texas	2	(2.4)
Washington	4	(4.9)
TOTAL	82	(99.7)*

*Total does not equal 100.0 due to rounding

more than one year of data will be needed to see if this continues.

ACKNOWLEDGMENTS

My thanks to Alexandra Morang and Janice Viticonte in the Office of Medical Student Affairs, Brown University School of Medicine for assistance in summarizing the data.

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Table 4
BROWN UNIVERSITY SCHOOL OF MEDICINE CLASS OF 1996 RESIDENCY POSITIONS

Name	Hospital Name/Medical School Affiliation	Specialty
Leah Adams	Rhode Island Hospital/Brown University	Internal Medicine
Meenakshi Aggarwal	NYU Medical Center/New York University	Internal Medicine
John Anastasatos	Presbyterian Hospital/Columbia University	Surgery-Prelim
Harry Aslanian	Mayo Graduate School of Medicine/Mayo Medical School	Internal Medicine
Marc Aversa	Valley Medical Center/University of Washington	Family Practice
Ilse Bell	Delaying Residency	
Richard Benoit	Harbor UCLA Medical Center/UCLA School of Medicine	Ob/Gyn
Sarah Boyl	Butler Hospital/Brown University	Psychiatry
Paul breiding	Miriam Hospital/Brown University	Internal Medicine
Mehri Brown	Memorial Hospital of Rhode Island	Family Practice
Manish Butte	PhD Program in Biophysics/Univ. of California, San Francisco	Delaying Residency
Christopher Camilleri	Harvard South Shore/Harvard Medical School	Psychiatry
Andrew Capraro	Univ. of Connecticut/Univ. of Connecticut School of Medicine	Pediatrics
Marina Catallozzi	Children's Hospital/University of Pennsylvania	Pediatrics
Geoffrey Chan	New England Medical Center/Tufts University	Internal Medicine
Steven Chang	Rush-Presbyterian-St. Luke's/Rush Medical College	Orthopedics
Alexander Chen	Cambridge Hospital/Harvard Medical School	Internal Medicine-Prelim
	Boston City Hospital/Boston University	Neurology
Joseph Chen	Mayo Graduate School of Medicine/Mayo School of Medicine	Internal Medicine-Prelim
	Mayo Graduate School of Medicine/Mayo School of Medicine	Phys. Med. & Rehab
Enoch Choi	Stanislaus Medical Center/CA	Family Practice
Norman Chou	Carney Hospital/Boston University	Transitional
Deus Cielo	Univ. of Texas Medical School/Univ. of Texas at Houston	Emergency Medicine
John Cribb	Rhode Island Hospital/Brown University	Internal Medicine
Christopher D'Arcy	Univ Washington Affiliate/University of Washington	Internal Medicine-Primary
Joseph Diaz	Rhode Island Hospital/Brown University	Internal Medicine-Primary
Heidi Dorris-Gorzewski	Miriam Hospital/Brown University	Internal Medicine
Alex Etienne	Norwalk Hospital/Yale University	Internal Medicine
Deirdre Fearon	Children's Hospital of Philadelphia/Univ. of Pennsylvania	Pediatrics
Katherine Frankel	Children's Hospital-Boston/Harvard Medical School	Pediatrics
Elizabeth Freedman	Univ. of Connecticut/Univ. of Connecticut School of Medicine	Family Practice
Jennifer Friedman	Research	Delaying Residency
John Gaitanis	Univ. of Rochester-Strong Memorial/Univ. of Rochester	Pedfiatrics
Rajiv Goel	Richland Memorial Hospital/Univ. of SC School of Medicine	Orthopedics
Robert Greer	Jewish Hospital/Washington University	Internal Medicine-Prelim
	Washington Univ -St. Louis/Washington University	Neurology
Robert Grossberg	Hospital of the Univ. of Pennsylvania/Univ of Pennsylvania	Internal Medicine
Rachel Guest	St. Louis Children's Hospital/Washington University	Pediatrics
Heidi Habicht	Memorial Hospital/Brown University	Family Practice
Mofiz Haque	Delaying Residency	
Timothy Hastings	Walter Reed Army Medical Center, Washington, DC	Orthopedics
Alexes Hazen	NYU Medical Center/New York University	Plastic Surgery
Agueda Hernandez	Greater Lawrence Family/Tufts University	Family Practice
Steve Ho	Yale-New Haven Hospital/Yale University	Surgery-Prelim
	Yale-New Haven Hospital/Yale University	ENT
Samuel Hostetter	Univ. of New Mexico School of Medicine/Univ. of New Mexico	Family Practice
Joseph Johnson	Evanston Hospital/Northwestern University	Internal Medicine
Melinda Johnson	Mayo Graduate School of Medicine/Mayo School of Medicine	Internal Medicine
Karin Kalkstein	Highland Hospital/University of Rochester	Family Practice
Edward Kim	Univ. of Southern Calif. Medical Center	Surgery-Prelim.
Eugene Kim	Mayo Graduate School of Medicine/Mayo School of Medicine	Internal Med.-Prelim.
Jinna Kim	Providence Family Medical Center/University of Washington	Family Practice
William Kim	Beth Israel Hospital/Harvard Medical School	Internal Medicine
Yeuen Kim	Santa Clara Valley Medical Center/Stanford University	Internal Medicine
Jihyun Koo	Boston University Med. Res./Boston University	Internal Medicine
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Gary Lai	LAC-USC Medical Center/Univ. of Southern California	Internal Medicine
Michelle Lefebvre	Rhode Island Hospital/Brown University	Pediatrics
Marilyn Li	Baystate Medical Center/Tufts University	Med/Peds
Carol Ling	St. John Hospital/Wayne State University	Surgery
Sandra Lora	Mt. Auburn Hospital/Harvard University	Internal Med.-Prelim.
	New York Eye & Ear Infirmary, NY	Ophthalmology
Karine Maalouf	Greater Lawrence Family/Tufts University	Family Practice
Robert McKittrick	Memorial Hospital of Rhode Island/Brown University	Internal Med.-Prelim.
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Catherine McLean	University of California-SF/UCSF School of Medicine	Internal Med.-Primary
Alexandra Meyer	Beth Israel Hospital/Harvard Medical School	Internal Med.-Prelim.
David Miller	Univ. of Chicago Hospital/Univ. of Chicago	Pediatrics
Carol Mimless	Memorial Medical Center of New Mexico/Univ. of New Mexico	Family Practice
John Miskovsky	Deaconess Hospital/Harvard Medical School	Internal Medicine
Melissa Murphy	Yale-New Haven Hospital/Yale University	Internal Med -Primary
Juel Nall	Frankford Hospital/Medical College of Pennsylvania	Transitional
Jeanne O'Brien	McGaw Medical Center/Northwestern University	Ob/Gyn
Scott Padavan	North Shore University Hospital/New York University	Emergency Med.
Teddy Pan	Beth Israel Hospital/Harvard Medical School	Internal Med.-Prelim.
Lara Penny	University of California-SF/UCSF School of Medicine	Family Practice
Sanjay Rao	MacNeal Hospital/Rush Medical College	Transitional
	Univ Southern California-LA/USC Medical School	Ophthalmology
Jennifer Retsinas	Univ. Texas Medical School/Univ. Texas @ Houston	Ob/Gyn
Victoria Reyes	Univ. of Washington Affiliate/University of Washington	Pathology
Colette Richards	Rhode Island Hospital/Brown University	Surgery-Prelim.
Rex Ruiz	Univ of Massachusetts Med. Ctr./Univ. of Massachusetts	Family Practice
Margret Rydell	Mayo Graduate School of Medicine/Mayo School of Medicine	Family Practice
Sanford Sineff	McGaw Medical Center/Northwestern University	Emergency Medicine
Brian Sites	Deaconess Hospital/Harvard Medical School	Surgery
Tyler Smith	Beth Israel Medical Center/Albert Einstein	Internal Med.-Primary
Robert Sokolic	Hospital of the Univ. of Penn/Univ. of Pennsylvania	Internal Medicine
Leslie Suranyi, Jr.	Rhode Island Hospital/Brown University	Internal Med.-Prelim.
	Dartmouth-Hitchcock Medical College/Dartmouth Medical School	Neurology
Julie Taitsman	Harvard Law School	Delaying Residency
Stacy Tessler	McGaw Medical Center/Northwestern University	Ob/Gyn
Deana Theroux	SUNY Health Sciences/SUNY Health Sciences Ctr. @ Syracuse	Pediatrics
Mark Vannorsdall	Maine Medical Center/University of Vermont	Internal Medicine
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Loryn Weinstein	Mayo Graduate School of Medicine/Mayo School of Medicine	Orthopedics
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MD2000: A Competency-Based Curriculum for the Brown University School of Medicine

Stephen R. Smith, MD, MPH and Barbara Fuller

Students matriculating into the Brown University School of Medicine in September 1996 will inaugurate an innovative curriculum that will break new ground in medical education both in the United States and around the world. The new curriculum, known as **MD2000,** defines a comprehensive set of competency requirements that all graduates are expected to attain.

The competency-based curriculum describes the knowledge, abilities, and personal values that define a successful graduate. Faculty determine if students have achieved mastery of these competencies through performance-based methods of assessment.

This article provides an overview of the reasons why the new curriculum was developed, what it hopes to accomplish, how it was developed, the ways it is structured, and the significance it will have for medical education. Four articles follow this one, each describing a major segment of the curriculum in more detail.

WHY IT WAS DEVELOPED

Several well-respected reports have criticized medical education over the last two decades. The General Professional Education of the Physician (GPEP) Report, published by the Association of American Medical Colleges (AAMC) in 1985, called on medical schools to give each student the knowledge, skills, values, and attitudes that all physicians should have. The report sharply rebuked medical faculties for overloading the curriculum with factual information that students were expected to memorize. "By this concentration on the transmittal of factual information, faculties have neglected to help [students] acquire the skills, values, and attitudes that are the foundation of a helping profession."[1]

ABBREVIATIONS USED

AAMC	Association of American Medical Colleges
GPEP	General Professional Education of the Physician

A report funded by the Macy Foundation highlighted deficiencies in the clinical education of medical students, noting that faculty rarely observed students directly to assess their ability to obtain a history or perform a competent physical examination.[2]

A more recent report by the AAMC reiterated the recommendations of the GPEP report and examined the reasons why implementation has been so slow.[3] Though all these reports seem to indicate a consensus among medical educators of what's wrong and what needs to be done, the lack of progress led one observer to describe the situation as one of "reform without change."[4]

The Robert Wood Johnson Foundation responded to these criticisms by launching a major funding program in 1989, the aim of which was to alter the infrastructure of medical education in fundamental ways that would lead to true change. Medical schools were invited to submit proposals for planning grants that would be awarded to twelve schools. Brown University School of Medicine was among those schools awarded a planning grant in 1990.

The leadership at Brown's medical school believed that "evaluation drives the curriculum." Change in the ways that medical students learned and medical school faculty taught would be more likely to occur if the outcomes of the whole enterprise were changed. Instead of solely determining whether students graduated based on the accumulation of course credits, graduation would be contingent upon demonstrating mastery of a defined set of competencies.

Research in other areas of education has shown that when the ways in which students are evaluated is changed, teaching and learning quickly conform to match the new expectations. Ronald Hardin, a medical educator from Glasgow, Scotland, relates a story about training soldiers to assemble guns in the field. Despite a well-presented curriculum in the classroom and good scores on their exams, the soldiers were not performing well in the field. A new teacher changed the way the student soldiers were tested. He cleared away all the desks and chairs and dumped disassembled guns on the floor. The soldiers were told that in order to pass the course, they needed to correctly assemble the guns. Soon all the students were on their hands and knees struggling with the equipment and the field manuals. The classroom instructors were right there next to them, helping them use the manual to guide the field assembly. Thereafter, the soldiers went into the field adept in assembling their guns.[5]

Granted, educating physicians is not the same as training soldiers how to assemble guns, but the principles are the same. Medical students are highly motivated learners. Medical faculty are dedicated teachers. Tell both of them clearly what is expected at the end of the educational process, and they will figure out a good way to get there.

By creating a competency-based curriculum, Brown medical school hoped to better assure that it was graduating physicians who possessed the qualities and attributes desired in a competent physician. Further, the new curriculum was expected to foster a sense of shared mission between student and teacher, both striving to reach a common goal.

The new curriculum would engender more active learning on the part of the students. Teachers would be more highly engaged in helping students gauge their progress and in identifying and overcoming barriers to their achievement.

This developmental process of teaching and learning is most effective when the milestones and end points are known. When known, the teacher and student can work together toward those shared goals, recognizing growth, identifying barriers, and collaboratively devising strategies to overcome those barriers. The teacher can create a learning experience in which students may practice those intellectual skills, examine their progress, incorporate discoveries, and practice again, all under the guidance, encouragement, and facilitation of the teacher.

With confidence that this model could truly reform medical education, the medical school embarked on designing a prototypical curriculum.

How It Was Developed

In 1990, teachers, deans, and students of the Brown University School of Medicine set out to paint a portrait of the successful doctor. From there they worked backwards to create a curriculum designed to produce that physician. The curriculum, published as *An Educational Blueprint for the Brown University School of Medicine,* has been dubbed **MD2000** because all graduates of the Class of 2000 and beyond will be expected to demonstrate competency in the knowledge and abilities outlined.

Planning the new competency-based curriculum differed markedly from the way medical school curriculums are typically designed. In most medical schools, the curriculum was shaped in a haphazard fashion, reflecting power struggles between departments over hours and courses. This often resulted in a curriculum that lacked an overall coherence and that often neglected important areas.

After listing the characteristics shared by the ideal physician graduate, the architects of **MD2000** spelled out nine abilities that should be expected of all medical school graduates (Table 1).The abilities range from those traditionally associated with good doctors, such as strong clinical and diagnostic skills, to other areas that are equally important but often overlooked – moral reasoning and ethical judgment, lifelong learning, social and community responsiveness, and personal growth.

Table I
BROWN'S NINE ABILITIES

I	Effective Communication
II	Basic Clinical Skills
III	Using Basic Science in the Practice of Medicine
IV	Diagnosis, Management & Prevention
V	Lifelong Learning
VI	Self-awareness, Self-care & Personal Growth
VII	The Social and Community Contexts of Health Care
VIII	Moral Reasoning and Ethical Judgment
IX	Problem Solving

Faculty and students translated each of these abilities into observable behaviors that students must demonstrate at the beginning, intermediate, and advanced levels of their training. Also developed were new methods of assessing competence in these areas – methods that rely on actual performance rather than on the traditional multiple-choice examinations. These performance-based methods of assessment include the use of standardized patients, interactive computer instruction, videotapes, and actual community health projects.

The knowledge base that was created to complement the abilities does not rely on a traditional disciplinary approach. Instead, nine interdisciplinary working groups of faculty and students determined what topics should be covered in the basic sciences, from the smallest level of organization – the cell and its molecular parts – to the largest level of organizationóthe community. Likewise, the clinical area focused on the many different types of meetings that occur between doctors and patients, from preventive visits to encounters in the emergency room (Figure 1).

Basic science matrix

Molecular/cellular	Single organ/ organ system	Whole person/ family	Community
Organization & structure			
Maintenance & homeostasis			
Defense against disease & injury			
Mechanisms of and response to disease & injury			
Therapies & interventions			

Clinical medicine matrix – Clinical approaches to health & disease

Preventive/ developmental	Acute	Emergency	Chronic	Behavioral
Fetus/Neonates				
Children				
Adolescents				
Adults				
Elders				

Figure 1 Knowledge base matrices (Each empty block presents a specific domain of knowledge)

Many have asked about the degree to which the proposed changes were resisted by the faculty. Initially, a number of faculty expressed skepticism about the

Table 2
MD2000 COMPETENCY ATTAINMENT GRID

Ability	Beginner Level	Intermediate Level	Advanced Level
I. Effective Communication	3	7	2
II. Basic Clinical Skills	3	5	2
III. Using Basic Science in the Practice of Medicine	8	6	2
IV. Diagnosis, Management and Prevention	3	7	2
V. Lifelong Learning	3	2	2
VI. Self-awareness, Self-care and Personal Growth	2	2	2
VII. The Social and Community Contexts of Health Care	2	2	2
VIII. Moral Reasoning and Ethical Judgment	1	4	2
IX. Problem Solving	5	3	2

plan. They believed that the present curriculum seemed to be working well and raised the argument that "if it ain't broke, don't fix it." Others expressed concern about the appearance of central control of the curriculum and erosion of academic freedom. Still others worried that the emphasis on competence and abilities conveyed an attitude that undervalued knowledge and science.

While the number of faculty expressing these sentiments never appeared numerous nor was their tone vociferous, the comments were taken seriously. The associate dean met with each department to explain the curriculum and answer questions. The "ain't broke" argument was easily refuted with hard data. Surveys of Brown students taken by the University of Massachusetts Medical School during a collaborative venture revealed that a sizable percentage of Brown students had reported never having been observed by a faculty member while performing a history and physical examination on a patient.[6] Clerkship directors readily admitted that no system was in place to guarantee that students acquired the clinical skills listed in the Educational Blueprint. Most basic science instructors would admit that they did not have any evidence that students could apply their basic science knowledge to clinical medicine.

Despite these data, the new curriculum was not presented as a radical cure for a seriously ill educational program. Rather, faculty were told that they were doing a good job – as good as most other medical schools – as evident from the success of the graduates in matching to excellent residency programs, receiving excellent evaluations from those post-graduate programs, gaining faculty positions at other medical schools in large numbers, and establishing successful practices here in Rhode Island and elsewhere. The new curriculum offered a way to do a good job even better. In the business world, the jargon used to describe this approach is "continuous quality improvement."

While the proponents of the competency-based curriculum believe it will dramatically change teaching, learning, and assessment, the new curriculum actually is less threatening to faculty who fear centralized control than other curriculum reforms employed in other medical schools. Unlike some reform efforts in which courses are broken up or merged with other courses into new configurations, MD2000 leaves the structure of courses and clerkships intact. Course leaders retain their authority to decide on the content of courses and the pedagogical methods, in contrast to schools where specific teaching techniques (e.g, problem-based learning) are mandated from above. Faculty are held accountable for the outcomes of their courses, but the details of how to reach those outcomes is left up to them.

The concerns about undervaluing knowledge and science were addressed by asking faculty to reflect on their own graduate education. The education that basic science Ph.D. faculty obtained was distinctly different from the traditional education of medical students. Graduate education relies much more on active, self-directed learning guided by faculty mentors. Knowledge is acquired as an inseparable part of the process of solving scientific problems, whose outcome is the creation of new knowledge. Likewise, for the expert clinician, knowledge is acquired as part of the process of solving clinical problems, whose outcome is the care of patients. Clinical investigators combine the two processes, caring for patients and advancing biomedical knowledge.

This method of graduate education contrasts sharply with the education of medical students who are expected to acquire huge quantities of facts largely in isolation. The use to which this information will be applied is referred to only in the abstract but with the admonition that it is essential in order to practice medicine competently. Students struggle to memorize and retain all this information out of fear that their patients will suffer irreparable harm, perhaps even death, should they forget even one fact. The task is, of course, impossible, which leads students to try to learn that information which is critical to the practice of medicine, of which they are ignorant. Sadly, in the end, students learn what they need to pass an examination.

The new curriculum seeks to transform medical education more into the mold of graduate education. The nine abilities specify the ways in which students will use the content defined in the knowledge base. Each course leader selects the appropriate abilities and aspects of the knowledge base and combines them in the teaching, learning, and assessment that is part of that course.

The confidence and support of faculty for the curriculum change was achieved by involving them actively in the planning process. Nearly 250 faculty, students, and administrators served on the 18 working groups that planned the curriculum. The entire faculty was invited to participate in a Delphi survey that achieved a final consensus on the knowledge base.

Title	**VII. THE SOCIAL AND COMMUNITY CONTEXTS OF HEALTH CARE**
Definition	**The competent graduate provides healing guidance by responding to the many factors that influence health, disease and disability, besides those of a biological nature. These factors include sociocultural, familial, psychological, economic, environmental, legal, political and spiritual aspects of health care seekers and of health care delivery. Through sensitivity to the interrelationships of individuals and their communities, the graduate responds to the broader context of medical practice.**
Criterion	1. Appreciates the importance of the many nonbiologic factors that influence health, disease, disability, and access to care
Behavioral cluster	• obtains information in the patient's history of these factors • attributes proper importance to identified nonbiologic factors • inquires about value systems and lifestyles in a non judgmental fashion • avoids stereotypical language (e.g., racist, sexist, or homophobic remarks) • identifies barriers to access of health care resources
Level of Achievement	**Level 1:** Beginner/novice students will meet the criteria for the social and community contexts of health care by recognizing and pursuing self-reflection of their own cultural and spiritual traditions, as well as gender, class and sexual socialization experiences. Students will be able to articulate ways in which these factors could influence their approach to medical practice. They will be able to recognize and discuss these factors when presented with material designed to highlight these issues, such as trigger tapes. Beginning students could familiarize themselves with the range of community services by visiting them, discussing the role of the agency with staff and clients, and observing the provision of services. Students could act as advocates by volunteering for community service even prior to having any medical training.

Figure 2 Anatomy of an ability in Brown's competency-based curriculum

DETAILS OF THE CURRICULUM

The three pillars of the new curriculum are the nine abilities, the knowledge base, and performance-based assessment.

ABILITIES

Figure 2 illustrates the "anatomy" of one of the nine abilities, namely *The social and community context of health care.* The Educational Blueprint defines each ability in a succinct paragraph, followed by a series of criteria that describe the desired performance of the student. Examples of behaviors that might be used by faculty to measure student competence are listed next. Finally, the level of achievement expected of students at the beginning, intermediate, and advanced stages of their educational development are described.

Most of the nine abilities follow this format. Ability II – *Basic clinical skills,* is somewhat different. It is a relatively long list of specific clinical skills, ranging from physical examination skills to routine clinical procedures, to complex and specialized laboratory and diagnostic tests. Each of the three levels of achievement specifies which of these skills the students are expected to be able to do and the level of proficiency. For example, beginning students are expected to be able to perform the basic elements of a history and physical examination prior to entering the clinical phase (third year) of their medical education. They are expected to perform these skills using proper maneuvers, form, and structure, though not necessarily in a smooth, efficient, or proficient manner. Beginning students are expected to be able to verbally describe the procedural steps necessary to carry out routine clinical procedures such as venipuncture, starting an intravenous line, and basic cardiopulmonary resuscitation. The students will have actually performed such procedures at least once, but would not be expected to be able to repeat them in a smooth, facile fashion at this stage.

KNOWLEDGE BASE

The knowledge basis consists of nine major divisions representing the column headings depicted in Figure 1. Outlines produced by each of the nine working groups underwent two rounds of review (using a consensus-building technique known as a Delphi survey) by volunteer faculty members. Items were rated on a scale ranging from *essential* to *not at all important.* The final database contains only those items (about three-quarters of the original items) receiving the ratings *essential* or *very important* by more than half of the participating faculty.

Inclusion in the knowledge base signifies the importance of a topic; all

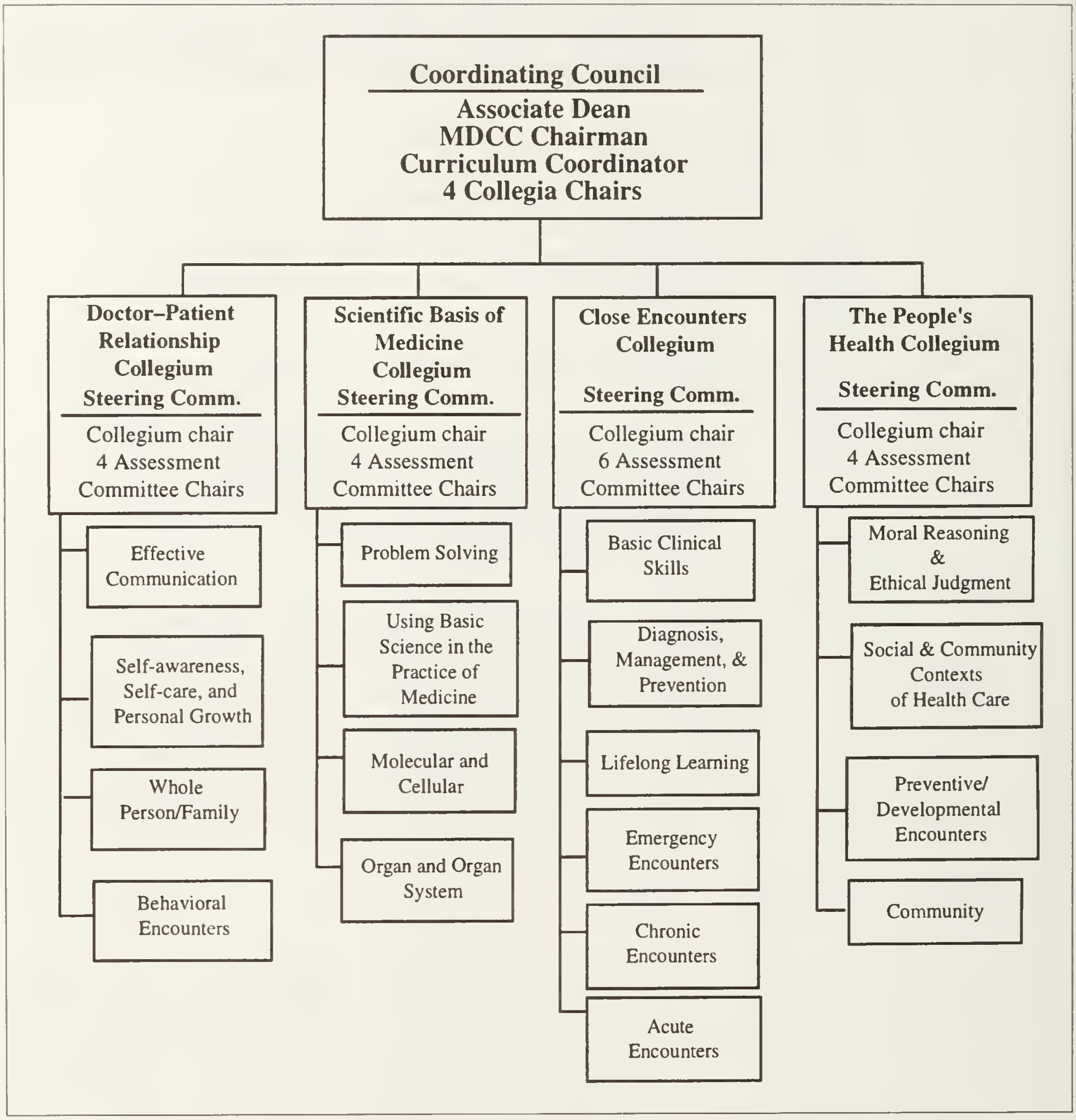
Coordinating Council
Associate Dean
MDCC Chairman
Curriculum Coordinator
4 Collegia Chairs
Doctor–Patient Relationship Collegium Steering Comm.
Collegium chair
4 Assessment Committee Chairs
Effective Communication
Self-awareness, Self-care, and Personal Growth
Whole Person/Family
Behavioral Encounters
Scientific Basis of Medicine Collegium Steering Comm.
Collegium chair
4 Assessment Committee Chairs
Problem Solving
Using Basic Science in the Practice of Medicine
Molecular and Cellular
Organ and Organ System
Close Encounters Collegium
Steering Comm.
Collegium chair
6 Assessment Committee Chairs
Basic Clinical Skills
Diagnosis, Management, & Prevention
Lifelong Learning
Emergency Encounters
Chronic Encounters
Acute Encounters
The People's Health Collegium
Steering Comm.
Collegium chair
4 Assessment Committee Chairs
Moral Reasoning & Ethical Judgment
Social & Community Contexts of Health Care
Preventive/ Developmental Encounters
Community

Figure 3 Organizational Structure for **MD2000**: Collegia and Assessment Committees

graduates should be able to use knowledge about that topic proficiently. A topic's exclusion from the knowledge base is not an indication of its irrelevance; rather, in planning the use of curriculum time, faculty assigned a higher priority to other topics that are in the knowledge base.

Many topics in the knowledge base intentionally permit wide latitude by the instructor in the selection of specific content with which to address the topic. For example, the knowledge base includes *genetics* under *mechanisms of disease* at the cellular and molecular level, but does not specify which genetic diseases or genetic abnormalities must be used to illustrate the principles. Faculty select specific content based on its teaching value according to prevalence, importance, general applicability, and particular illustrative value. Faculty are advised to present sufficient examples to make general principles clear, but to avoid going beyond this objective. Faculty are also urged to select content that is relevant to the practice of medicine.

Performance-Based Assessment

The goal of teaching is to help the student to learn. In order to do so, the teacher and the student must know how well the student is doing in reaching the educational outcome desired. Assessment is the process by which the teacher and the student gain knowledge of the student's progress. In our competency-based curriculum, we want to create assessments that reflect as closely as possible the actual tasks that students will face as physicians. These assessments need to be authentic and direct. We call this performance-based assessment.

Performance-based assessment requires the student to use knowledge in a particular way to satisfactorily complete the task assigned. Students will not be able to perform satisfactorily if they lack either the knowledge or the ability. The knowledgeable student who is unable to integrate knowledge to diagnose a patient's problems will not perform satisfactorily when confronted with a patient with a complicated history, vague physical findings, and confusing laboratory data. Nor will the student who has excellent communication skills do any better if he or she does not know what clues to look for in the history. Competence requires the simultaneous application of knowledge and ability.

The four articles that follow in this issue describe examples of how the three pillars of the curriculum – the nine abilities, the knowledge base, and performance-based assessment – are combined in teaching, learning, and assessment in the medical school curriculum.

IMPLEMENTATION PLAN

Assessment committees have been formed corresponding to the nine abilities and nine divisions of the knowledge base. Each committee consists of about six faculty members and two students.

The assessment committees do not directly assess students. Instead, they monitor the process by which faculty assess students. Each course or clerkship is empowered by the assessment committee to certify student competence in that area. In order to be so empowered, the course or clerkship director must meet with the assessment committee to describe the methods by which student competence in that area will be assessed. The course leader will also describe how the course is structured and conducted to enable students to reach the learning goals.

Once a course has been empowered to certify student competence, the assessment committee will expect the faculty to rigorously evaluate how well their assessment plans are working and present progress reports to the committee. The purpose of these progress reports is primarily to engender collegial conversations, brainstorm new ideas, and creatively problem-solve rather than to monitor compliance.

Rarely, assessment committees may determine that the faculty member has not undertaken a good faith effort to employ performance-based methods of assessment. In that case, the assessment committee may deauthorize the course's ability to certify student competence. That will mean that students taking the course will not be able to obtain certification for that ability.

Instead of solely determining whether students graduated based on the accumulation of course credits, graduation would be contingent upon demonstrating mastery of a defined set of competencies.

Each student must attain competence in all nine abilities and across the entire knowledge base. Among the abilities, students must attain an intermediate level of competence in all nine, and an advanced level of competence in problem solving and three others of the student's choice.

To attain competence, students must receive a minimum number of certifications of competence in the ability in which competence is being sought (Table 2). For example, the student must receive four certifications in effective communication at the beginning level (level 1) to be designated competent in Ability I at the beginning level. For the knowledge base, a single certification is sufficient for that content area.

It is possible for a student to pass a course, fulfill the knowledge base requirement, and still not receive certification for competency in a particular ability. For example, a student could pass the human morphology course, thus fulfilling knowledge base requirements under the single organ/organ system division for gross anatomy, but not be deemed competent in effective communication – one of the two abilities assessed in that course.

Assessment committees are grouped together in one of four competency collegia (Figure 3). The chairpersons of the assessment committees and the chairperson of the collegium meet together as a steering committee to plan faculty development workshops. Each collegium is responsible for planning and hosting one faculty development workshop annually.

In addition to the annual faculty development workshop, the medical school supports travel for faculty to attend programs related to their teaching and offers curriculum development grants.

SIGNIFICANCE FOR MEDICAL EDUCATION

The authors believe that Brown's competency-based curriculum represents the prototype for medical education in the next century. The current model of medical education, based on Abraham Flexner's famous report in 1910, served medicine well by building the education of medical students on a firm scientific foundation. A new model of medical education is needed now to prepare today's graduates to face the challenges ahead. Flexner himself presaged the need to consider the broader needs of a comprehensive medical education. He wrote:

> So far we have spoken explicitly of the fundamental sciences only.... The practitioner deals with facts of two categories. Chemistry, physics, biology enable him to apprehend one set; he needs a different apperceptive and appreciative apparatus to deal with the other, more subtle elements. Specific preparation is in this direction much more difficult.... [T]he physician's function is fast becoming social and preventive, rather than individual and curative. Upon him society relies to ascertain, and through measures essentially educational to enforce, the conditions that prevent disease and make positively for physical and moral well-being.[7]

Brown's approach to the education of medical students begins with the tasks that will be expected of the physician practicing in the twenty-first century, then builds a curriculum designed to equip its graduates with those attributes needed to competently perform those tasks. Residency programs will know that an M.D. degree from Brown means that graduates have been taught, have learned, and have been assessed competent in these outcomes.

Other medical schools in this country and around the world are likely to follow Brown's lead. Two other U.S. medical schools have adopted the Brown model wholesale. Copies of the educational blueprint have been requested from 10 medical schools in Europe, Australia, and Asia.

Recently, the AAMC announced a major new project called the Medical School Objectives Project, the goal of which is to develop a consensus among the medical education community on the objectives of the medical school experience. Once this is done, the program will help medical school faculties reform their educational programs to achieve these outcomes.[8] Brown's curriculum will serve as a model for others to study in planning their own competency-based curriculums.

The articles that follow, written by the chairpersons of the four competency collegia, describe real examples of how the competency-based curriculum is already being employed in their respective areas.

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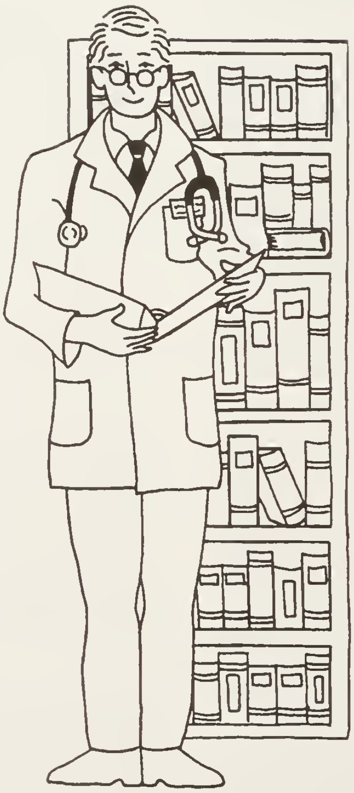

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The People's Health Competency Collegium

Esther J. Entin, MD

THE VISION

Scene I: The doctor has completed her physical examination of her patient. She has reached a diagnosis and treatment plan but realizes that lab work and prescriptions are only part of the solution. From information in her patient's social history, she is aware that she must address his access to the lab and radiology department. She knows that he is reliant on friends and family for rides and that he does not like to impose upon his peers. She stresses the urgency of these studies, makes a mental note to look into the availability of cab vouchers with the help of the social worker. She makes sure the patient will bring a translator with him or that the hospital is notified of this need. She would like a Visiting Nurse to visit her patient to follow up on his progress because she has learned that he does not have a phone, but she is aware from the patient's socioeconomic-class experiences of his potential discomfort with a home visitor and takes care to discuss at length the role the nurse will play.

This doctor is aware of this broadened context of medical therapeutics and has the skills to identify the nonmedical factors that will impact upon this patient's illness, compliance and recovery. She knows how to use the social/health care system and how to communicate this knowledge to the patient because she has been specifically taught, mentored and evaluated in these skills during her medical school experiences.

Scene 2: The doctor sits on a hospital committee which is discussing a drug company's offer to financially support a hospital conference. Although the economics are appealing, the ethical issues are complex. Some of the physicians see no problem in accepting drug company's funding as long as appropriate information is given to participants. Others are irate at their colleagues' willingness to be subliminally manipulated by this advertising. In addition to having a gut feeling about the issue, the doctor is able to explore the ethical implications, using paradigms of ethical decision making which he learned during his medical school training. Although there is no right answer, the committee meeting is a satisfying experience because he has helped the group apply systematic ethical analysis to work through an emotionally charged subject.

The doctor is able to do this because he was specifically taught, mentored and evaluated in these skills during his medical school experiences.

Scene 3: The doctor is performing a pre-employment physical. Although she has a brief form to fill out which focuses on past medical history, current medications and current health problems, she questions her patient at length about his diet, his smoking and alcohol and drug habits. She screens for mental health status, aware that depression may accompany financial stress, cause family disruption and may promote substance abuse, risk taking behavior, and undermine success in the work place. She questions him about his sexual behavior, educating the patient while she is screening for risk of HIV exposure and other sexually transmitted diseases. She asks about the environment of his work place, stressing his right to OSHA standards, and the importance of learning about the correct operation of machinery as well as the availability of first aid and safety equipment. She feels a sense of satisfaction that she has contributed more to this patient's life than a simple medical clearance for job application. She hopes that she has established an ongoing relationship with this patient, made her interest and advocacy clear to him and perhaps provided him with some information which may encourage healthful changes in his life.

She is able to do this because she has been specifically taught, mentored and evaluated in preventive health issues as part of her medical school training.

THE PAST

The topics of the social, cultural and community-related implications of health care, the need for ethical decision making, and the tenets of preventive health care are not new concepts in medical education. They have been taught at Brown as well as medical schools all around the country for years. Indeed, because of their inherent link to illness, wellness, compliance and outcome, these issues have been inevitably present in the medical school curriculum from its inception. Discussions in classrooms and on ward rounds, during case presentations and social histories as well as Grand Rounds and Ethics Rounds have always provided the students with exposure to the multifaceted nature of medical practice. However, this content has usually been serendipitous, and the educational message incomplete. Specific educational/behavioral objectives have not been routinely determined for these areas. The faculty has not been responsible for identifying precisely how they teach, mentor and evaluate the student's achievement of such skills. But perhaps most significant, the demonstrated mastery of behavioral and educational objectives in these disciplines has never been a requirement for graduation equal in importance to passing basic sciences, clinical clerkships and other standard rotations.

THE PRESENT

As described by Dr. Smith in his introductory article, the **MD2000** Curriculum, in a document titled *An Educational Blueprint for the Brown University School of Medicine,* has formalized a set of behavioral objectives and a knowledge base of information. The document has come from the painstaking delineation of the desired outcomes of a student's education at the Brown medical school. Using this document as a guidebook, the medical school curricu-

ABBREVIATION USED

OSHA — Occupational Safety and Health Administration

ADDITIONAL ILLUSTRATIVE MATERIAL ON EACH OF THE FOUR COLLEGIA AREAS FROM THE *EDUCATIONAL BLUEPRINT*

The Social and Community Context of Health Care

Criteria for Assessment:

1. Appreciates the importance of the many non biologic factors that influence health, disease, disability and access to care.
2. Utilizes appropriate resources in the community that may provide support for reducing social causes of disease.
3. Acts as an advocate for better health for patients and the community.

Moral Reasoning and Ethical Judgment

Criteria for Assessment:

1. Understands basic ethical concepts and applies them in moral reasoning in the medical and health care context.
2. Recognizes the ethical dimensions of medicine.
3. Identifies the conflicting ethical considerations in a particular ethical choice.
4. Systematically analyzes and defends ethical choices in the treatment of an individual patient.
5. Determines, articulates, and analyzes the ethical issues in health policy.
6. Determines, articulates, and analyzes the ethical issues in relations with other health care professionals.
7. Identifies relevant case and statutory law bearing on ethical issues and choices; analyzes and defends positions abut its role in ethical choices.
8. Demonstrates and employs skills necessary to implement ethical choices in medical practice.
9. Effectively integrates the above ethical skills in the care of his or her own patients.

Community Knowledge Base: (abbreviated from Blueprint. Each item is further delineated in an extensive outline form within the Blueprint.)

A. Structure of the U.S. Health care system
   1. Financial and organizational structures
   2. Financial and organization structures of competing organizations and their roles
   3. Current stresses on U.S. health care financing

B Public Health methodologies and policies
   1. Public health, epidemiology and biostatistics
   2. Public policy and health policy

C. Issues in the health care system
   1. Availability and accessibility of medical care
   2. Costs
   3. Quality and acceptability
   4. Special population group issues
   5. Practice issues

D. Prevention
   1. Chemical, immunological environmental approaches
   2. Behavioral
   3. Political and regulatory interventions designed to enhance community health

Preventive/Developmental Encounters Knowledge Base(abbreviated from Blueprint. Each item is further delineated in extensive outline form in the Blueprint.)

1. Function and development
2. Nutrition
3. Mental health
4. Substance abuse
5. Sexual behavior
6. Accidental injury
7. Occupation and environmental health
8. Specific diseases
9. Specific age group related issues

EACH of these items is further defined with age-appropriate information and is applied through the life cycle: infancy, childhood, adolescence, adults, elders, and pregnancy.

lum is being examined through a new lens. Both faculty and students now have a blueprint to apply to existing courses as well as to the creation of new courses, educational experiences and evaluation strategies. They have a map for making it all happen reproducibly and purposefully. This massive undertaking has been organized into a hierarchy of coordinating committees with each ascending level given ever more expansive charges and each descending level given the luxury to focus and refine a manageable piece of the whole. The entire Blueprint (curriculum) has been divided into four competency collegia. Each collegium is the functional working unit for 4-6 curricular segments including both abilities and knowledge base items. Through the development years and now through the implementation years, the collegia remain the basic organizational units which make it possible to work effectively within this massive body of competencies and knowledge.

The People's Health Collegium

The People's Health collegium coordinates and evaluates courses that will certify students in two of the nine abilities, and two subdivisions of the Knowledge base. The knowledge base outlines the large body of didactic information which is considered a critical mass for the graduating student to assimilate. The two abilities describe specific behavioral skills which require the student to translate the factual knowledge into informed action. The abilities and knowledge base are both distinct and interrelated, as the expression of the abilities relies on the knowledge base for informed action and the knowledge base relies on the abilities for itís appropriate and meaningful application in the clinical setting.

The following descriptions of the abilities and knowledge base coordinated by the People's Health collegium are somewhat abbreviated from the Educational Blueprint. More detailed information from the Blueprint can be found at the end of this article and even more in the Blueprint itself.

The Social and Community Contexts of Health Care (Ability VII)

The competent graduate provides healing guidance by responding to the many factors that influence health, disease and disability, besides those of a biological nature. These factors include sociocultural, familial, psychological, economic, environmental, legal, political, and spiritual aspects of health care seekers and of health care delivery. Through sensitivity to the interrelationships of individuals and their communities, the graduate responds to the broader context of medical practice.

Moral Reasoning and Ethical Judgment (Ability VIII)

The competent graduate recognizes the ethical dimensions of medical practice and health policy, identifies alternatives in difficult ethical choices, analyzes systematically the conflicting considerations supporting different alternatives, and formulates, defends and effectively carries out a course of actions that takes account of this ethical complexity. The graduate combines a willingness to recognize the nature of the value system of patients and others with commitment to his/her own system and the ethical choices necessary to maintain his/her own ethical integrity.

Community Knowledge Base:

A. Structure of the US health care system

B Public Health methodologies and policies

C. Issues in the health care system

D. Prevention

Preventive/Developmental Encounters knowledge base

Function and development, nutrition, mental health, substance abuse, sexual behavior, accidental injury, occupational and environmental health, specific diseases and specific age group issues are all applied through the life cycle: infancy, childhood, adolescence, adults, elders, and pregnancy.

Redefining traditional course boundaries and stressing interdisciplinary regrouping and inter-relatedness of medical education highlight the MD2000 curriculum. The four described competencies and knowledge bases are not exclusively present in courses certified by the People's Health collegium, nor do the certified courses exclusively teach these highlighted competencies and didactics. Quite the contrary, the entire medical school curriculum has teaching elements, mentoring opportunities and opportunities to demonstrate mastery in the wide spectrum of the nine abilities and nine knowledge areas. However, this collegium to the assigned specific responsibility for its four curricular charges to those courses whose course leaders had a desire and a methodology for emphasizing the People's Health themes both in their teaching and in their student evaluations in a focused and reproducible fashion.

The Educational Process

Key to the educational mission of the MD2000 curriculum is the notion that the experience (volunteer work, case presentation, etc.) is not enough. The intentional and educational processing of the student's experiences with his/her peers and mentors provides the educational key to influencing future medical practice habits. Similarly, it is not simply the reproduction of knowledge base items from notebook to test paper that reveals the student's mastery of information. Thus both the teaching and the evaluation methodologies implicit in a competency-based curriculum diverge from traditional paper and pencil, multiple choice and essay tests. Such experiences and opportunities will complement the existing medical educational framework of lectures, lab work, small group didactic sessions, clinical ward rounds and case presentations.

An Example: In order to achieve certification in the knowledge base and competency skills of Community and *Ability VII – The Social and Community Contexts of Health Care,* a student may elect a service- learning project Along with a group of peers, she may assess the health needs of a local community, develop an educational plan to meet those needs, and then present it to the community members. During this process the students will face their own attitudes towards different communities, discover the communication skills that are necessary to keep the balance between talking down yet being informative. They will learn to approach community members and win their trust, learn to approach physician mentors and obtain their guidance. They will experience the realities of transportation, child care, safe meeting places, and scheduling that are inherent in community education projects. They will discover how it feels to stand up before a group as the expert. During this process, they will work with peers and with mentors to face both the medical/educational issues for the community and their own personal growth issues. They will obtain feedback on their meetings with community members and on their presentations. Their volunteer work will expand far beyond the traditional definition to meet their own agendas as well as the community's.

Years later, as physicians in communities and practice settings of all sizes, they will call upon the skills that they learned, remember communication issues, remember assessment skills, remember the positive feelings engendered by their participation in such community outreach. Their medical education will take them out of their offices and into their patients' communities with ability and with great confidence.

Another example: To work toward an ethics competency certification, a student may write a paper discussing the ethical issues involving in a patient he worked with on a ward rotation. Although clinical rotations may not be specifically labeled as ethics courses, the student may choose to address the issues of a patient on any of his clinical rotations. He may meet with a physician/ethicist mentor to discuss his paper while in progress. The mentor may recommend readings about medical ethics or about similar cases. The student will face his own emotional responses and learn to reconcile them with the intellectual structure of ethical thought. He may discuss the case from this point of view with their ward team, eliciting the opinions of the housestaff and attendings. The clinical team will be lucky to have this perspective added to their busy and diagnosis-focused rounding.

Years later, the student – now physician – when faced with a troubling ethical dilemma, will remember the algorithms of moral reasoning, will remember to both separate and combine the emotions and the intellect, will know how to approach hospital ethicists and interdisciplinary institutional committees and engage in meaningful dialogue and will feel competent to help a patient, family and colleagues make difficult decisions.

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And yet a third example: To encourage a demonstration of mastery in Preventive Health Care, a preceptor in an outpatient setting may assign a student the project of counseling a variety of age groups about the risks of injuries and accidents. The student will research the various threats to life and limb ranging from toddler accidents, to teenage behavior, to adult drinking , to firearms in the home, to risk factors for falls in the elderly population. He will be asked to raise these issues with real or simulated patients and to develop efficient yet effective counseling methods to be used during brief clinical encounters. He will be mentored on developing a language and presentation style which is appropriate for his patients' varying levels of education and sophistication. He may research existing patient educational material, determine its usefulness, including its availability in other languages, or develop his own patient handouts.

Years later the student – now physician – will routinely and efficiently incorporate this important aspect of prevention counseling into his care giving and will have the skills and the knowledge to develop other prevention related patient interventions.

THE YEAR 2000+

In practice settings, academic medical settings, and physician organization meetings all around the country and world, Brown graduates of the MD2000 curriculum bring a confident knowledge, broadened perspective, and ability to employ behaviors which reflect competence in nontraditional medical skills and cross-disciplinary knowledge. Their practices will reflect their expanded concept of health and disease, their facility with dilemmas calling for moral reasoning and ethical judgment, and their vision of the role of the physician in the community as a health care provider for individuals and as an advocate for groups. They will be advisors on disease prevention at an individual and societal level and will take an active role in community health issues.

Our graduates will be able to do this because they were specifically taught, mentored, and evaluated in these areas during their medical school experiences with The Peopleís Health collegium.

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The Scientific Basis of Medicine

James M. Gilchrist, MD

"The Scientific Basis of Medicine" is one of the four competency collegia convened by Dean Steve Smith in the fall of 1993. The name then was "The Cutting Edge: Scientific Applications in Medicine." I like the present title, which has been adopted through ad hoc usage, because it is shorter and more to the point. Within this collegia are two of the nine Brown abilities, and two of the nine knowledge bases: Ability III – using basic science in the practice of medicine and IX problem solving, and knowledge bases "molecular/ cellular" and "single organ/organ system."

Much more so than any of the other competency collegia, this one is concerned with medical education in the first two years, the basic science years of lecture halls, laboratories, and all-nighters studying for midterms and finals. In a lot of ways, this is the collegia where the success of **MD2000** will take root or die. The concept of performance-based, competency evaluation is a long way from the multiple-choice test which is the heart and soul of the evaluation process of most basic science courses during medical education. The first two years of medical education are largely rooted in the didactic lecture hall, with sojourns to laboratories for supplementary experiences. This method of teaching medical students is certainly time-tested, having been a mainstay of medical education for a thousand years, and is not to be superseded as a device for conveying large amounts of information within a limited period of time. And as form follows function, the multiple-choice test is hard to challenge as a method for testing large amounts of information given limited time and manpower. And here is the dilemma, how to inform medical students of the ever-increasing amount and complexity of medical basic sciences while keeping in mind we wish them to be good doctors, not good test-takers.

ABBREVIATIONS USED	
OSCE	Objective Structured Clinical Exam
SCIM	Structured Clinical Instruction Module

It is with this thought in mind that **MD2000** was developed, to define what we want Brown medical graduates to know and be, and to then design their education to meet that goal. Thus, the delineation of the knowledge bases and of the abilities. And continuing to work backwards, if one accepts that the best way to teach someone to play baseball is to have them play baseball rather than to give them a series of lectures, then it becomes clear that the best way to teach medical students to be doctors, is to have them successfully perform the skills we wish them to have. Thus, performance based evaluation of competence. This then requires methods of evaluation in which students exhibit their competence in the desired skill rather than simply taking a paper test. In turn, this requires a method of impartng information other than the didactic lecture. So while the beloved course names of histology, microbiology, physiology, et al may not change, the content, the didactic tools and the evaluation methods are certainly going to differ.

Each course must also now take on the task of evaluating for 1, 2 or 3 of the Brown abilities. To fully understand how **MD2000** will affect these core courses, the reader should realize both knowledge base and Brown ability requirements must be met, and their evaluation and satisfactory completion are independent. It will be possible to pass a course's knowledge base for example, human histology, but not satisfactorily display competence in an ability also evaluated in that course, such as problem solving. This does not require retaking human histology but does mean that the required experience in problem solving will have to be met in some other way.

Within the nine abilities are criteria to be used for assessment, listed in the Educational Blueprint, as well as three levels of achievement beginner, intermediate and advanced. For Ability III – Using basic science in the practice of medicine, a Brown medical student will be required to satisfactorily complete eight experiences/courses at the beginner level, six courses/experiences at the intermediate level, and two experiences at the advanced level. This is the most heavily represented ability of all nine, indicating how important an understanding of basic science is to successful medical practice. Fortunately, among the core medical curriculum of the first two years, there are 14 courses (virtually all of which are the basic medical science courses also necessary to meet knowledge base requirements) which have been chosen to evaluate for Ability III, eight at the beginner level and seven at the intermediate level. Learning experiences at the advanced level for this ability will likely be accomplished through independent study, research projects, clinical presentations and writing case reports.

A good example of assessment of competence in a basic science course by performance evaluation is the first year course in Human Morphology, profiled by its course director, G. E. Goslow, in the January 1996 issue of *Medicine & Health/Rhode Island*.[1] Professor Goslow has chosen three Brown abilities to evaluate: Ability I – Effective communication, Ability V – Lifelong learning and Ability III – Using basic science. Aside from the actual testing of the knowledge base during practical and other exams, the students are required to present prosection demonstrations, viewed by a panel of instructors and a visiting expert, which "focus on a region of anatomy ... and are centered on some clinical, functional or evolutionary point." The topic must be related to the clinical or basic scientific literature. Feedback is given shortly thereafter, with each student evaluated for quality of prosection, use of outside resources and understanding of the underlying structures and functions. Thus, for Ability III – Using basic science, students at the beginner level should be able to recognize and articulate a general conception of health and disease based on normal function and pathophysiology.

At the intermediate level, the student should have a coherent understanding of the molecular, cellular and physiologic aspects of disease, and integrate this into a therapeutic management plan, including the mechanism of action of drugs, side effects, and indications. A good example of a course evaluating for Ability III at the intermediate level is BI 262–Neurologic Pathophysiology, taken in the second semester of the second year. Again, the knowledge base is assessed by quizzes and exams, and the ability is evaluated by demonstration of competence, via small group sessions. The initial sessions utilize case vignettes for lesion localization, which the students are required to demonstrate and explain to the faculty preceptor and the other students. The next two sessions utilize neuropathologic slides, which are presented to the students for their description, and then explanation, of the underlying pathophysiology and subsequent clinical sequelae. The final five sessions tie it all together by again utilizing case vignettes in which students synthesize and present the localization, pathophysiology, diagnostic evaluation and management of a variety of neurologic diseases.

The other ability within the scientific basis of medicine collegia is Ability IX – Problem solving. Requirements for graduation include five courses/experiences at the beginner level, three at the intermediate level and two at the advanced level. There are currently six courses in the core curriculum of the first two years of medical education at Brown which evaluate for the beginner level of Ability IX, as does one 300-level course and several of the affinity groups. The clerkship in family medicine has decided to take on the responsibility of assessing for problem solving at the intermediate/advanced level. This illustrates one of the challenges facing implementation of **MD2000:** the dearth of course options for students to accomplish the intermediate level of Ability IX, a scarcity which is not unique to this Brown ability and which will need to be addressed creatively. A beginner student should be able to identify and solve problems of a straightforward or unidimensional nature. Two brief examples illustrate the variety of approaches to accomplish this. Dr. Michael Glantz, first in an affinity group and then in a course funded by the teaching scholars committee, guided students through the process of identifying a medical problem to investigate, researching the issue, proposing a hypothesis and developing an experimental plan. In BI 372–Human Development in Health and Illness, students in small groups use clinical cases as a platform to identify selected biological, psychological or sociocultural problems impacting upon the patient, to research and report back. In addition, the students write a one-page case formulation. The intermediate student in Ability IX should be familiar with the knowledge base and be able to summon other of the Brown abilities, to solve problems of greater depth and breadth. In the family medicine clerkship, a clinical objective structured clinical exam (OSCE) which integrates identification of health problems with diagnosis, management, prevention and communication is used to assess competence in problem solving at the intermediate level. For example, a standardized patient, trained in the OSCE format, will present a family history of coronary artery disease, as well as a personal history of cardiac risk factors. The student would be assessed on their ability to elicit the appropriate history, formulate a management plan to appropriately address the risk factors, and communicate with the patient regarding the plan. One of the interesting aspects of such an evaluation plan is that the "patient" also participates in the assessment and in the feedback of the medical student.

> *... not only is a new style of curriculum being promulgated but that new, additional skills are to be acquired and assessed, skills possibly more akin to art than science.*

The core basic medical curriculum encompassing the first two years of medical school as it has existed at virtually all American medical schools for the past several decades is to largely to cover what the Brown Education Blueprint now calls the "Molecular/Cellular" and "Single Organ/Organ System" knowledge bases. The challenge before us is less one of assuring adequate coverage of these knowledge bases but of finding evaluative, and by connection, didactic methods in which to assess competence in the acquisition of the information. As above, the multiple choice test is inadequate to the task, and creative solutions including case-based learning, such as in medical microbiology, problem-based learning, such as in biochemical pharmacology, and structured clinical instruction modules (SCIMs) are already being used. New tools of teaching, including technology such as video, CD-ROM and hypertext need to be investigated as do new concepts of teaching such as the "triple-jump exam."[2] In this method, to use a physiologic example, on day one students review a paper "case" in class, listing relevant physiologic issues, justifying the inclusion of two of the issues by short essay and identifying one for further research. That completes the first "jump."[2] In the second "jump," over the next week the student does a literature research over one week on the selected physiologic topic from the case, and writes a one-page summary. The third "jump," on the last day of the week, is a series of essay questions about the physiology of the case, tailor made to fit the topics identified by each student in the first "jump." This is obviously just one of several potential methods (and a rather labor-intensive one) to evaluate knowledge base acquisition utilizing performance-based assessment.

The Brown medical curriculum is at a crossroads, but the direction it will take is clearly down the path of performance-based, competency evaluation. Medical school courses will remain hybrids for the next few years, combining features of both the old and the new teaching and evaluative methods. It my hope, and that of the **MD2000** steering committee, that the faculty will embrace this new curriculum, and hasten to assist in the transition. The reader must bear in mind that not only is a new style of curriculum being promulgated, but that new, additional skills are to be acquired and assessed, skills possibly more akin to art than science. These new abilities are very important, as any practicing physician will attest, such as communication with patients and family, moral and ethical reasoning, and problem solving, but have not been formally evaluated in a medical curriculum before. This is one of the more exciting aspects of MD2000, but in that excitement we must not lose sight of the accomplishments of the past nor of the multiple purposes of medical education. The responsibility of the competency collegium The Scientific Basis of Medicine is to ensure its title reflects reality. No matter what the method, and regardless of the curricular style, our graduates must be as well-versed in the science of medicine as they are in the art of medicine. It is my personal belief that MD2000 represents a new paradigm in medical education, another step in evolution from mythology, apprenticeship and scientific laboratory, and is our best shot yet at accomplishing the complete education of physicians.

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A Panoply of Patient Encounters: The Close Encounter Collegium

Peter S. Smith, MD

Translating a conceptual blueprint on how the Brown medical student functions effectively in close encounters with his patients may be daunting. The items listed in *An Educational Blueprint for the Brown University School of Medicine* document are many and might lead one to expect a staggering amount of knowledge and abilities before encountering, talking with, thinking about, examining and managing the care of people entrusted to his care. Featured in the document are dozens of pages listing hundreds of items making up the content for the abilities and knowledge base the graduating student must handle competently in order to fulfill the ideals embodied in the MD2000 curriculum. Yet we must bear in mind that a blueprint cannot and does not represent the final product of a major enterprise: in architecture, as in other endeavors, it is a working draft, by nature flexible, from which one derives the larger landscape. In this essay I will articulate what the mission of the Close Encounters collegium is, the tasks it will perform and the role of its constituent assessment committees in implementing the curriculum outlined in *An Educational Blueprint for the Brown University School of Medicine.*

The mission of the Close Encounters collegium is to develop learning environments which foster the attitudes and behaviors in medical school graduates, enabling them to achieve optimal encounters with patients under all the circumstances likely to occur in clinical practice. The existing Brown medical curriculum consists of many traditional lectures and courses often modified by simple accretion of new knowledge. Some of them have served their purpose marvelously and have remained fairly intact over the years. Others have been updated significantly because of advancements in the science of medicine. But in general too many of our courses have heavily relied on traditional book knowledge, to the detriment of experiences dealing with the richness of live patient encounters in clinical practice.

The Close Encounters collegium is Brown's response to this need. It builds upon the best parts of the existing preclinical and clinical courses and expands them to include and to assess abilities in all kinds of encounters with people seeking services from the medical system. The assessment groups, which make up the Close Encounters collegium cover the whole range of doctor meeting patient. The groupings are based upon the emphasis of the encounter. In the basic clinical skills assessment group, members will focus on the knowledge and abilities to perform the types of examinations and procedures common to all of the medical fields and their specialties: the physical examination, the performance of routine clinical procedures. This group will also monitor to what extent the graduate will have observed and become familiar with the indications and complications of more advanced clinical procedures such as percutaneous liver biopsy, and endoscopy. Another assessment committee will oversee and monitor the courses which deal with diagnosis, management and prevention – a fundamental part of any medical curriculum – generally offered by the clerkships and clinical electives. The prevention aspect of this assessment group will probably represent the greater challenge, since encounters with a focus on prevention are mainly in ambulatory and outpatient settings in which there is often less structure.

How do our graduates develop a pattern of continually updating their familiarity with medicine and its context? The assessment committee on lifelong learning will find ways to assure that courses, even at the beginner's level, integrate skills promoting continuous learning. A subcommittee of the medical curriculum committee is already looking into ways to familiarize students with the technological advances that enable them to retrieve data rapidly and with ease from their computer. Workshops to foster a favorable and knowledgeable reception of these innovations by faculty are planned as well. The tasks of the three other assessment committees will encompass the abilities and knowledge the competent graduate must muster in each of three types of clinical situations of differing nature and acuity: acute encounters, chronic encounters and emergency encounters.

A hypothetical clinical paradigm illustrates the knowledge and abilities that are represented in the Close Encounters collegium

A 17 year-old-male is brought by ambulance to the emergency department after a head-on collision with another car. He is obtunded, wears a bracelet identifying him as a diabetic, and smells of alcohol. He groans about his chest hurting. What are the required abilities a graduate must have to assess and manage this patient? What courses at Brown provide the student with the knowledge and skills to deal appropriately with this scenario? The assessment committee on emergency encounters will be aware of the courses at Brown and in its affiliated hospitals which offer knowledge and clinical experience in acute trauma. With the help of the Educational Blueprint committee, members will define and prioritize what the graduate must know and be able to perform in order to competently care for acute trauma cases. Members will scrutinize each course or clerkship which lists the emergency encounters as an area of focus for evidence that the requisite knowledge and skills are actually taught. They will monitor the process by which faculty assess students by inviting the course leader to describe the methods by which such competencies are demonstrated. In this instance a graduate of our medical school will be able to rapidly perform an assessment of the state of consciousness of this patient, his respiratory functioning and the need to intubate and ventilate should he develop respiratory failure.

There will of course be overlapping areas with the assessment group on acute encounters, which justifies periodic meetings of the steering committee of assessment group chairs to coordinate work, avoid duplications and disparity of assessment tools and strive for agreement on principles and priorities of the process. For instance the acute encounters knowledge base, includes among adolescents injuries and suicide attempts within its purview. Is this a course redundancy which should yield to neglected competencies, or is such overlap an advantage due to the issue's inherent importance and prevalence?

This same scenario could be used to illustrate the role of the assessment committee on Ability IV – Diagnosis management and prevention. A number of courses at Brown address alcohol abuse and some clerkships, such as pediatrics, have strong prevention components against trauma, accidental poisoning and communicable diseases. It stands to reason that a graduate must be able to demonstrate competency in these areas and that assessment of these abilities be assured. What aspects of trauma are covered by these courses, and how does the clerkship director demonstrate that the student knows how to diagnose alcohol addiction? What will the committee require in order to empower course leaders and clerkship directors to certify competency in these skills?

In identifying resources which help deter alcohol abuse and dealing with adolescent defiance, the assessment committee on Ability V – Lifelong learning might look into how a course imparts facility and measures competence in retrieving information on community resources for troubled adolescents. Resources range from the obvious, like the yellow pages and knowledgeable preceptors, to the more detailed national and local computerized data bases. The assessment committee will rigorously evaluate how well courses certified in lifelong learning integrate content enabling the student to not only frame a question, but also use modern information searching techniques.

Just as crucial here are issues related to a chronic disorder in this adolescent, diabetes mellitus. How many graduates feel they have the know-how to effectively differentiate between acute alcohol intoxication and diabetic ketoacidosis in this adolescent, and what would be the appropriate management pending the results from the laboratory? The assessment committee on chronic encounters assures that courses offering education in chronic diseases do in fact deal and assess the student's knowledge and ability in addressing people with such diseases. Awareness concerning predictable medical crises, developmental and psychosocial issues, developing a long term care plan, and enabling patients and their families to manage most aspects of their own care must be fostered in our graduates. Armed with the course numbers listing these kind of encounters, members of the assessment committee will draw upon course outline, syllabi, course leader descriptions and evaluations by medical students to establish that course content and listed abilities and knowledge base coincide.

> *Awareness concerning predictable medical crises, developmental and psychosocial issues, developing a long-term care plan, and enabling patients and their families to manage most aspects of their own care must be fostered in our graduates.*

The scope of the Close Encounters collegium includes many of the most traditional elements of a medical curriculum. What will set it apart at Brown is the degree to which it will be able to assure that the knowledge base and clinical acumen developed over a finite number of years will be translated into competencies which go beyond a familiarity with techniques and facts. Assuring that our graduates are indeed adept dealing with the complexities their patients bring to the encounter will be the ultimate proof of success in creating well-rounded and accomplished physicians.

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Doctor-Patient Relationships: Know Thy Patient, Know Thyself

Lucile F. Newman, PhD and Lynn Epstein, MD

"To write prescriptions is easy, but to come to an understanding with people is hard."

Franz Kafka, *The Country Doctor*

While it is a given that doctors need to offer their patients the latest knowledge and skill, it is clear that such technical skill is of scant value unless framed within a social context. At the Brown University School of Medicine, an underlying premise is that medicine is a socially responsible human service profession. This premise has a direct impact on the core abilities, on the elements of the knowledge base, and on the clinical experiences, which together constitute the medical education curriculum. Hence, the social nature of medicine includes the recognition of communication and interpersonal skills as central components of effective medical care.

Effective interactions with colleagues, staff, patients, and the public are essential skills for all physicians, regardless of specialty or practice setting. Similarly, an important task of medical education is to inculcate in students a recognition of the ever-present need for clear, compassionate communications with those who are ill, in pain, elderly or dying. Conversations, whether with colleagues or with patients, involve listening as well as speaking.

At Brown, the Doctor-Patient Relationship collegium is made up of two large categories from the knowledge base (or subject matters), namely The Whole Person/Family, and Behavioral Encounters; and two abilities (or basic understandings), namely *Effective Communication,* and *Self-Awareness, Self-Care and Personal Growth.* Together, they constitute an emphasis on the personal development of doctors and on effective interaction with others, which is central to becoming a well-educated physician. The goals of this collegium include fostering the *individual* (i.e. a self-aware person, who is also part of a family), and fostering the *interaction* (i.e. behavioral encounters characterized by effective communication).

One of the important contributions of medical education is helping students to recognize the continuing need for clarity, compassion, and respect for diversity in their communications with those who are ill, in pain, or dying. In order to begin to foster a knowledge base in the area of Behavioral Encounters, one must truly comprehend another, whether patient or colleague. It is only through an understanding of the developmental dimensions of the person who is the patient, that it is possible to engage the patient as a partner in healing, and to know the person apart from the disease. It is not always easy to understand the patient's complaints, since what is painful or difficult may be only the symptom of a basic problem. In addition, patients do not always understand or follow the recommendations their physician offers. It is therefore apparent that communicative care includes both listening and explaining in order to assure the patient's belief in the efficacy of recommendations and in the possibility of recovery. Forming this kind of therapeutic alliance is essential to the effective management of care.

Similarly, the Whole Person/Family recognizes that all individuals come from family and ethnic groups and have origins and lives beyond being a patient solely with medical concerns. Students in relationships with patients and their families need to respect and take into consideration the values and tenets of these groups. As well, communications and recommendations can be tailored to the needs of the individual. To achieve these ends, the competency-based curriculum of MD2000 emphasizes educational outcomes involving active learning methods and requires creativity in course design and teaching.

EDUCATIONAL STRATEGIES

During the undergraduate years of education, competency in these knowledge bases is achieved in part through courses such as family sociology, writing and English, mathematics, identification and criticism of ideas, basic physical sciences and social sciences. In medical school, competency is attained through courses and experiences, with the thought processes, unique to the sciences. At Brown, the diversity of learning experiences is a strength and takes students beyond strictly clinical training.

Competency in both communication and self-awareness can also be achieved through non-course experiences, through active learning, innovative direct experience in Affinity Groups, behavior change or collaborative research projects, or in community service activities, all of which enable students to learn while working together with others.[1]

ACTIVE LEARNING

One of the broadest educational innovations, as described in the AAMC's report, *A New Vitality in General Education,* concerned the importance of what was termed "active learning."[2] Active learning includes any activity that engages the student in primary experience, followed by reflection on and interpretation of that experience. There are many formats for active learning. Students may work with faculty in course development, as teaching assistants, in research projects, and as undergraduate writing fellows, or as mathematics or science advisors. All of these activities involve close collaboration with a faculty member and are particularly effective in introducing the student to new conceptual systems – no longer as a passive learner, but as an active participant in the process of teaching as well as learning. There are numerous opportunities on a college campus for teaching assistantships.

Robert Sternberg, describing an experiential theory of intelligence, wrote, "Intelligence is best measured by tasks that are 'non-entrenched' in the sense of requiring information processing of kinds outside people's ordinary experience".[3] According to this view, intelligence is not so much a person's ability to think within conceptual systems that have already become familiar, as it is his/her capacity to learn and think within new conceptual systems that can be brought to bear on already existing knowledge structures. Active learning thus provides a context of experiences that contribute to self-awareness and personal growth as well as to the acquisition of knowledge and skills. It plays a prominent role in the approach to learning for the collegium on doctor-patient Relationships as exemplified by the philosophy and approach to student learning in the Affinity Group Program.

Affinity Groups

The Affinity Group Program at the Brown University School of Medicine links small groups of 8-10 students together with two faculty or staff members in a longitudinal advising and educational program which spans a four-year period from the third undergraduate year through the second year of medical school. First implemented in 1987, each group reflects the interests of its participants and combines personal and professional interactions in formal and informal settings.[4] One of the novel features of the program is this emphasis on core goals and objectives which focus on process rather than content. Individual groups are thereby able to be creative in developing their "affinities," and they have pursued a wide range of areas and activities, such as: international health; community-oriented primary care; public health; health care organizations; issues of ethnic or cultural diversity; doctor/patient relationship; stress management; health care for specific groups or specialties – women's health, health care needs of the elderly, pediatrics, psychiatry; use of humanities disciplines in medicine; the impact of technology; and research. Affinity Groups provide a format for early clinical experiences, community interactions, and the pursuit of creative learning opportunities.

What all have in common is the small and supportive group format within which students develop their own plans, explore their commitment to medicine, become aware of their values and biases, develop skills in problem-solving, self-directed learning, communication and the use of resources.[5] The group provides a model of self awareness and communicative abilities over time, in which students learn to assess themselves and each other accurately and to give and receive constructive criticism.[6] During the four-year period, the program builds a hierarchy in problem-based learning, which expands from the usual case-based format to work with standardized patients and then to a focus on the larger, systemic aspects of problems and options for solutions.[7] Many of the affinity groups participate in service-learning, thereby making contributions to patients, agencies and the community at large.[8]

> *Students need to be in tune with their personal identity, to cultivate a reasonable personal expectation for the successful management of stress, and to develop the explicit ability to respond appropriately to constructive feedback.*

In the context of Brown's new competency-based curriculum, Affinity Groups play an important role in meeting early competency requirements in many of the abilities, such as: *Effective Communication; Lifelong Learning; Self-Awareness, Self-Care, and Personal Growth; Social and Community Contexts of Health Care; Moral Reasoning and Ethical Judgment;* and *Problem Solving.*[9] Faculty and program consultants have identified together those abilities and their levels, which the program addresses regardless of the specific interest area. In addition, because of the four-year sequence of the program, affinity groups play an important role in helping to integrate abilities and knowledge acquired from other courses. In addition, as groups pursue their areas of interest and curricular projects, they can address other abilities, knowledge areas and extend the level of competency. Taken together, the program provides a structure to foster student development both personally and professionally.

Dimensions of Personal Development

Communication and Listening Capacity

As mentioned earlier, in the back-and-forth dialogue we call communication, active listening is an essential element. Implementation includes dyadic and group work, as well as interviewing and patient interaction. Gaining the confidence of another person is vital to the ability to communicate on complex and intimate issues. In clinical settings, understanding the situation of the person who is the patient enhances understanding of that person as well as the presenting problem.

The first level of interviewing takes place with students interviewing each other in the affinity groups. The interviewing course begins formally in the first year of medical school by "shadowing" a clinician, or going on rounds with a faculty member to understand how that person approaches interviewing a patient. The anatomy course in the first year of medical school at Brown is innovative in that students act as collaborators in analysis of issues of anatomy, and report a group on their findings to the class; in essence, learning to work together, rather than competitively. This course is described in the January 1996 issue of *Medicine and Health/Rhode Island.* Collaborative projects are also used in many advanced science courses, and the communicative functions in these courses provide experience for the students in both eliciting information and speaking about it.

Interviewing takes on a more directed format during the second year of medical school, when students combine their interviews with physical diagnosis. It is expected at this point that students have acquired the communication basics and are able to interact effectively and compassionately with patients. Their tasks at this point relate to a focused history and review of systems. During the last two years, while in specific clinical rotations, students have the opportunity to interview patients in a variety of settings as they are exposed to different medical disciplines.

The second level for interviewing is that of the objective structured clinical exam (OSCE) format with simulated patients. Trained volunteers play the part of a patient with a particular configuration of symptoms or concerns, and evaluate each student on their ability to elicit the relevant description during an interview.

SELF-CARE, SELF-AWARENESS AND PERSONAL GROWTH: THE BEHAVIOR CHANGE PROJECT

Much of the opportunity for improved health care depends on an ability to encourage patients to make health-improving changes in their lives. Based on the understanding that, as a physician, one's efforts will often be directed to encouraging a patient to change risky behaviors, a Behavior Change Project in the first year of medical school enables students to understand just how difficult it is to change their own risk-related behaviors. Beginning with definition of a personal goal, a focused physical examination, and interview with a consultant to establish what areas of change would be most needed, the student designs and undertakes a project to change, over the three months of the semester, the identified risk behavior. This could range from a diet change to reduce cholesterol, to an exercise regimen, to weight loss or gain, relaxation techniques, or a change in sleep habits.

A final physical examination and interview assess the degree of change in behavior and in risk factors, and a final paper focuses on student reflection about the experience, its difficulties and successes, and its meaning for self-awareness, self-care, and personal growth.

CONCERN FOR OTHERS: COMMUNITY SERVICE

Community service enables a person to participate in activities that serve others, in the process, learning to give and receive appropriate feedback. Experiences in community service provide another form of "learning by doing" in which a student can participate in improving the health of the community through involvement in a particular clinical situation, social service agency, or any voluntary groups engaged in addressing problems of illness, poverty and disadvantage.

Many students volunteer, or undertake internships or group projects in community-based agencies. Some of the agencies may act as a "try-out" of a particular area for the student's future work, such as volunteering at a gerontology center, or a children's hospital. Others reflect a commitment to the community through regular volunteer work and concern with particular issues, such as an AIDS Hotline, or a homeless food provision service. Community service activities augment competency-based medical education.

Personal documentation of performance in informal interviewing, community service, behavior change, and other non-course experiences may be kept as an electronic portfolio, providing a record as varied and intrinsic to medical education as formal course experiences, as well as providing a documentation of personal growth.

CONCLUSION

The process of becoming a physician is a challenging one. Students are faced with an extensive set of knowledge bases to master, as well as with the acquisition of vital skills and abilities. Central to the task is the relationship between doctors and patients, which also asks students to have intimate knowledge of themselves as well as their patients. The abilities of *Effective Communication* and of *Self-Awareness, Self-Care and Personal Growth* challenge students to make effective use of the subject matter they have learned. Expectations for achieving competencies are different for the various levels of medical education. A first level undergraduate is encouraged to self-awareness and reflection regarding, for example, the organization of time which is an essential ability for both medical school and future practice. Similarly, an important aspect of self-care and personal growth is learning to balance priorities, to manage stress, and to learn from experience. Students need to be in tune with their personal identity, to cultivate a reasonable personal expectation for the successful management of stress, and to develop the explicit ability to respond appropriately to constructive feedback.

The medical school graduate develops these forms of behavior. While caring for patients is a responsibility, it is also a privilege. As such, simple facts are easier to acquire than are the confidence, self-esteem and an understanding of people. Knowledge is of most use to doctors when they enlist patients as partners in healing.

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Health by Numbers

Rhode Island Department of Health
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Edited by Jay S. Buechner, PhD and William J. Waters, Jr., PhD

Lyme Disease in Rhode Island: Three Years of Surveillance

Matthew C. Nicholson, PhD, Thomas N. Mather, PhD, and Edward F. Donnelly, RN, MPH

Dr. Nicholson is a post-doctoral associate at the Center for Vector-Borne Disease, University of Rhode Island. Dr. Mather is associate professor of entomology and director of the Center for Vector-Borne Disease, University of Rhode Island. Mr. Donnelly is senior public health epidemiologist, Division of Disease Prevention and Control.

Background. Lyme disease is a definitive example of an emerging infection. First recognized as a distinct malady in 1977 from a geographic cluster of patients in Lyme, Connecticut, it has become the most commonly reported vector-borne disease in the United States.[1] Caused by infection with the bacterium *Borrelia burgdorferi*, Lyme disease is associated with tick bites. In the northeastern United States, the Lyme agent is transmitted from animal reservoirs to humans by a bite from the black-legged tick, *Ixodes scapularis*, which is also known as the deer tick.

Although human risk for Lyme disease is related to the density of Borrelia-infected ticks in the environment and the degree of human contact with tick habitats, little is known of how these tick populations, and thus Lyme disease risk, vary geographically and with time. Since 1993, the Rhode Island Department of Health and the Center for Vector-Borne Disease, University of Rhode Island, have conducted statewide surveys of tick populations in conjunction with the active surveillance program for Lyme disease in humans. The objectives of these surveys have been to delineate black-legged tick populations in the state both geographically and numerically, to track tick population trends over time, and to correlate these measurements with human infection.

Methodology and Results. Most human cases of Lyme disease occur during summer months when the poppy-seed-sized nymphal ticks are active. Thus, surveillance efforts have focused on assessing nymphal tick populations in the state. In Rhode Island, peak activity of nymphal I. scapularis occurs around mid-June. Each year since 1993, at least 80 forested locations across the state have been surveyed.[2] Each location was visited twice between late May and mid-July, and tick populations were surveyed by collecting 90 "flag-samples" at each visit. "Flag-samples" consisted of dragging 0.5 meter^2 white flannel flags across the leaf litter and collecting all ticks attached at 30-second intervals. With this technique, the tick population density at a site was estimated by the

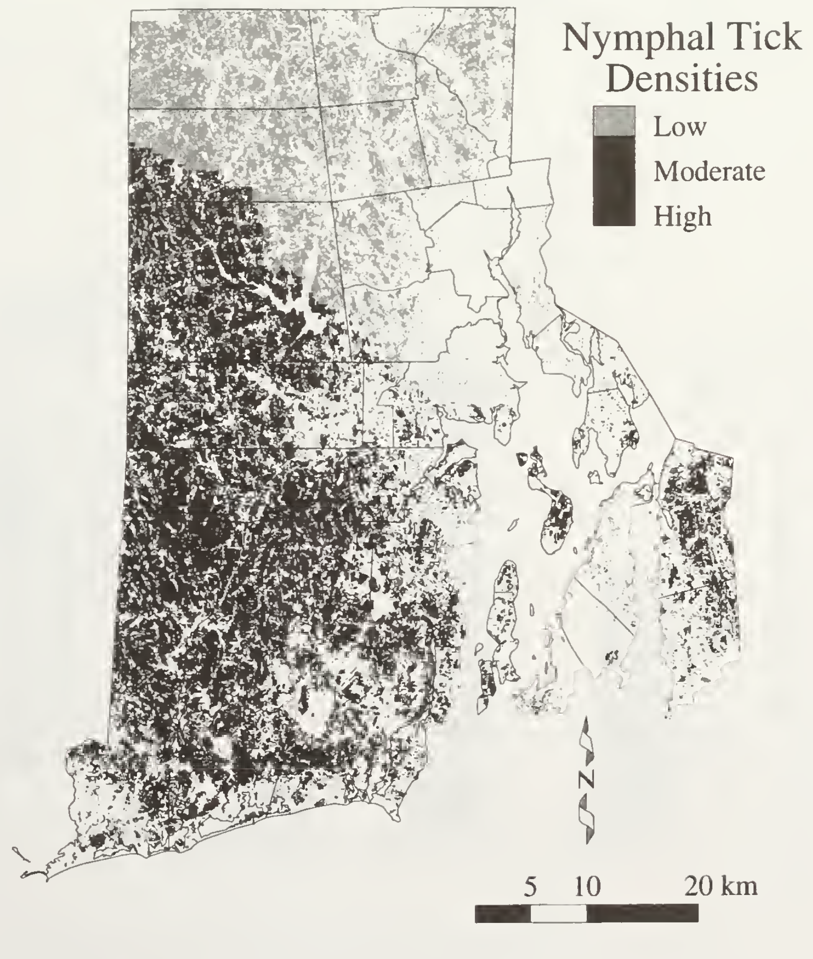

Figure 1 Estimated density of nymphal I. scapularis, Rhode Island, 1993.

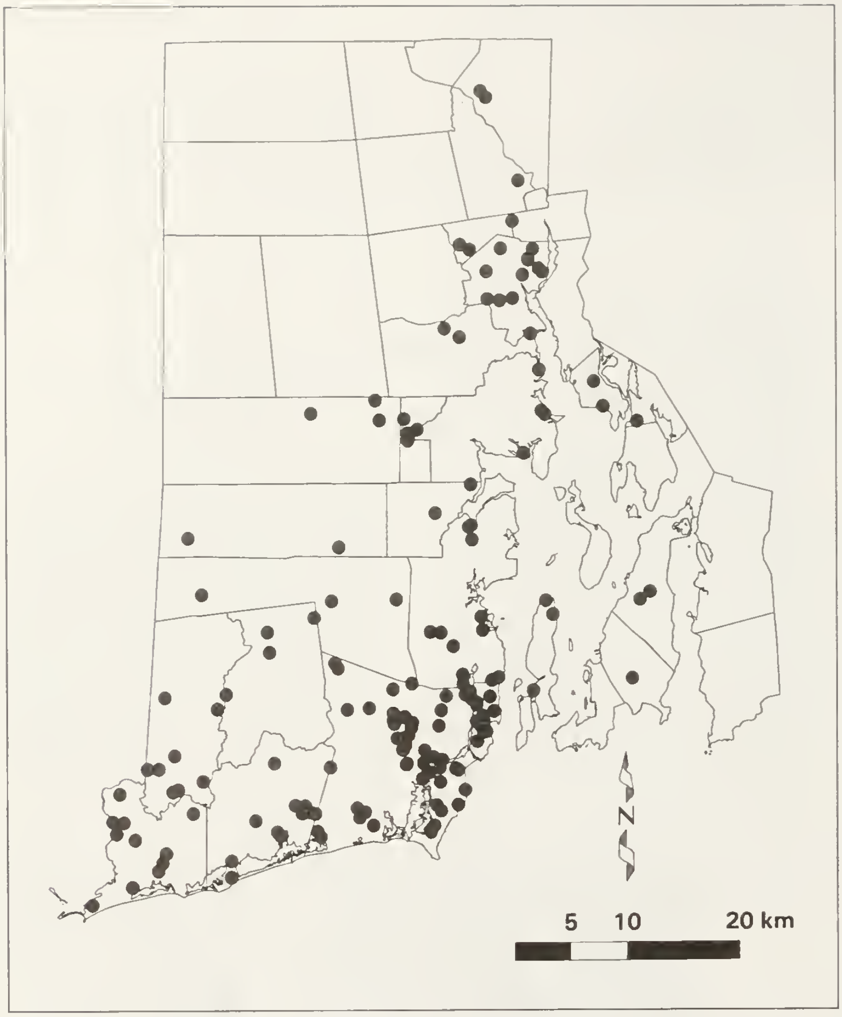

Figure 2 Place of residence for reported cases of Lyme disease, Rhode Island, 1993.

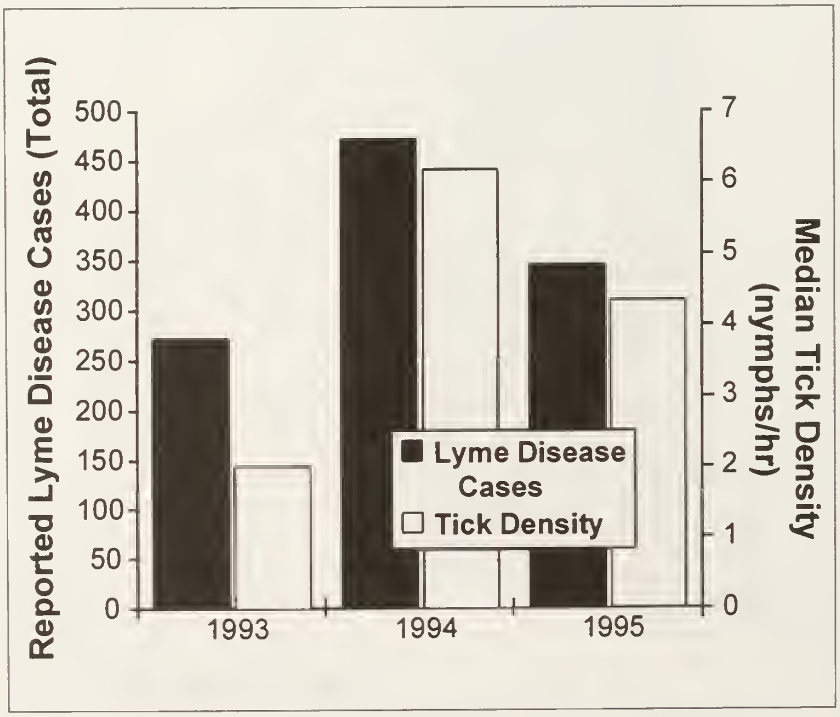

Figure 3 Statewide median density of nymphal I. scapularis and number of reported Lyme disease cases, Rhode Island, 1993-1995.

number of nymphal black-legged ticks collected per hour of sampling.

Spatial analysis techniques were used to extrapolate site-specific tick densities and estimate state-wide distributions of nymphal I. scapularis populations. Figure 1 illustrates that the areas of highest tick density are found in southern Rhode Island west of Narragansett Bay and on Prudence and Block Islands. In order to determine the association between local tick abundance and Lyme disease risk in Rhode Island, a geographic information system was used to map the home residence of Lyme disease cases reported to the Department of Health. Included were only those cases with complete address information provided on the case report form. Figure 2 depicts the results of this mapping effort for 1993; each circle represents one case report. (To assure patient confidentiality, locations on this figure are accurate to approximately 2 kilometers.) It should be noted that the geographic distribution of reported cases was similar in 1994. There are clearly more case reports from the southern portion of the state than elsewhere. Comparing Figures 1 and 2, it becomes evident that high tick densities are spatially associated with Lyme disease reports. Furthermore, trends in the number of Lyme disease case reports over the three years of observation closely follow the corresponding statewide median tick density (Figure 3).

Discussion. Several newly emerging infectious diseases, like Lyme disease, are tick transmitted. Within the past two decades, populations of the northern black-legged tick, *Ixodes scapularis*, have greatly expanded their range and degree of human contact. Because of their catholic bloodfeeding habits, these ticks very likely will be responsible for emergence of other zoonotic infections, in addition to Lyme disease, as their populations expand both numerically and geographically. Already, an increasing prevalence of human babesiosis, which is caused by infection with the rodent piroplasm, *Babesia microti*, has been observed. More recently, it has been discovered that the pathogen causing the newly recognized human granulocytic ehrlichiosis (HGE) shares a similar natural history with the Lyme disease agent.[3,4] Rhode Island's tick surveillance program is facilitating our understanding of health risks posed by the emergence of tick-borne zoonoses. For now, it would appear that the factors regulating densities and geographical distributions of this particular group of ticks also impose limits to the distribution of human disease risk caused by a wide array of zoonotic pathogens.

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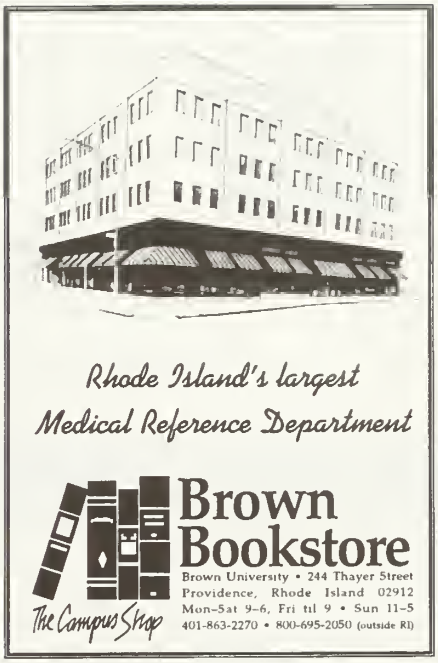

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Vital Statistics

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Roberta A. Chevoya

Rhode Island Monthly Vital Statistics Report
Provisional Occurrence Data from the Division of Vital Records

Vital Events

	Reporting Period		
	Feb. 1996	**12 months Ending with Feb. 1996**	
	Number	**Number**	**Rates**
Live Births	1,095	13,573	13.6*
Deaths	774	9,665	9.7*
Infant	(4)	(91)	6.7#
Neonatal	(1)	(69)	5.2#
Marriages	333	7,434	7.5*
Divorces	214	3,555	3.6*
Induced Terminations	526	5,714	421.0#
Spontaneous Fetal Deaths	78	1,046	77.9#
Under 20 weeks gestation	(77)	(985)	72.6#
20 + weeks gestation	(1)	(61)	4.5#

* Rates per 1,000 estimated population
# Rates per 1,000 live births

Underlying Cause of Death

	Reporting Period			
	August 1995	**12 Months Ending with August 1995**		
	Number (a)	**Number (a)**	Rates (b)	**YPLL (c)**
Diseases of the Heart	231	3,324	3323.6	4,496.5
Malignant Neoplasms	222	2,458	246.7	7,103.5
Cerebrovascular Diseases	44	628	63.0	540.0
Injuries (Accident/Suicide/Homicide)	35	365	36.6	5,042.0
COPD	22	409	41.1	347.5

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.
(b) Rates per 100,000 current estimated population of 996,325.
(c) Years of Potential Life Lost (YPLL).

Note: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

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Ninety Years Ago

August, 1906

H.G. Patridge, MD describes 56 cases of puerperal eclampsia which had come to his personal attention during the preceding 3 years. He first reports the impressions of others, beginning with Zweifel's observations that the "disease is due to a poison formed within the maternal organism and circulating in the blood." He also quotes Ewing's observation that the disease is frequently accompanied by severe liver disease. In passing he notes: "Several writers have stated that the blood pressure is very greatly increased in eclampsia... We have made no observations as to this in any of our cases although many of them presented a so-called tense pulse." He then comments on the use of saline injections in eclampsia and wonders, since so much edema accompanies the disease, whether saline administration is wise. He concludes with a brief synopsis of such measurements as the frequency of eclampsia [1 in every 28 deliveries], frequency of convulsions, time of onset and mortality rate [41.1%]

The Journal reports on a splendid banquet given to honor Dr. J.W.C. Ely on the sixtieth anniversary of his entrance into the practice of medicine in Providence. Letters of congratulation from many distant places were read to the audience including a lengthy note from William Osler. A loving cup was presented to Dr. Ely by his many colleagues and admirers. The evening was concluded by a talk by Dr. Ely in which he recalled his days at Brown [Class of 1842] and Harvard Medical School [Class of 1846]. Harvard, then, occupied a small building at the end of a dingy alley, surrounded by tenements in downtown Boston. The faculty numbered fewer than ten, and the only clinical experience consisted of a weekly session of observation at Massachusetts General Hospital. Ely opened his Providence office in the spring of 1846. Office visits were 25 cents while house calls were 50 to 75 cents. Ely then described the character of medical practice, both inpatient and ambulatory in those distant years, and the many students he took under his wing in the days when medicine could still be learned by apprenticeship. He concludes with a quotation from the Rector of Aberdeen University: "Genius has no place in medicine; even cleverness is not to be encouraged. Men who gain distinction in medicine must possess the following qualities: self-reliance, capacity for continuous hard work, close observation, kindness and honesty; and that they should be dogmatic when they thoroughly understood the subject." One month after the banquet, on May 6, 1906, Dr. Ely died.

Fifty Years Ago

August,1946

The surgical management of carcinoma of the colon and rectum is outlined by Thomas E. Jones, MD, describing the clinical course of 137 consecutive cases supervised over an interval of 20 months. No immediate fatalities were listed although 8 of the patients had visible liver involvement, 25 had atherosclerotic heart disease and 4 were diabetic. The bulk of the paper is devoted to the merits of modified interventions designed to minimize the possibility of ensuing peritonitis.

Russell S. Bray, MD describes his experiences with gastritis among Navy personnel at Newport Naval Hospital. He discusses the various elements associated with gastritis in young personnel - some physical, many psychological - and concludes that many such sufferers become "gastric invalids" and thus are incapable of rendering service to the armed forces.

The conservation of pulmonary function in the treatment of chest casualties is discussed by David B. Jennison, MD. He concludes: "Metal foreign bodies should be removed only when there is an indication that their presence will cause complication in the future. The mere presence of a foreign body is not disqualifying for duty. Hemothoraces should be aspirated early and frequently enough to keep the pleural cavity dry and the lung fully expanded. Emphyemas that are localized, small and have an underlying lung that is capable of fully expanding or empyema in the patients too sick to stand a decortication are treated by open drainage."

On the anniversary of 15 years of service, the Journal describes the facilities, and educational opportunities provided by the Bradley Home, a children's psychiatric hospital.

TWENTY -FIVE YEARS AGO

AUGUST,1971

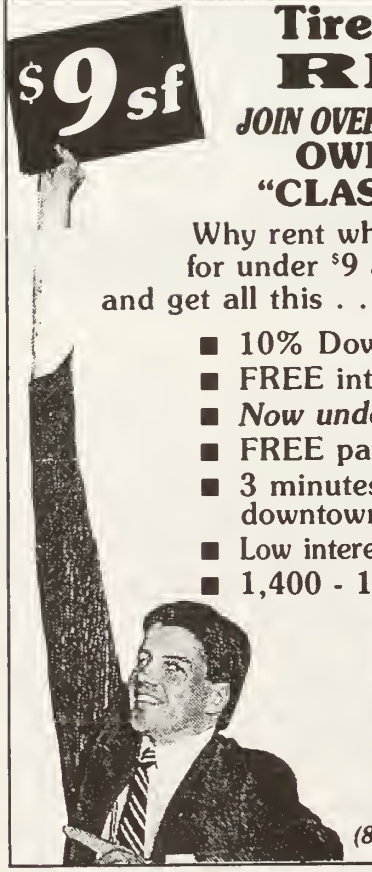
Congressman Robert O. Tiernan [2nd District, Rhode Island] discusses health care from the Washington vantage point, considering in detail such legislative proposals as the Murray-Wagner-Dingell Bill, the Nixon proposal, the Kennedy-Griffiths proposal and the Javits plan.

Eli Ginzberg, PhD, Chairman of the National Manpower Advisory Committee, discusses the sense and nonsense of hospital costs. "The only chance of moderating the cost increases that lie ahead is for third parties to design and exercise controls so that the producer cannot continue to charge whatever he wants to charge. For this. . . we need pre-expenditure controls."

Seebert J. Goldowsky, MD and Ezra Sharp, MD present a case study of a 67 year old woman with jejunal diverticulosis. The authors discuss the diagnostic features of a disorder which may mimic various metabolic illnesses and may be the cause of idiopathic anemia and hypoproteinemia.

Banice M. Webber, MD, MD discusses the relationships and responsibilities between hospital and physicians emphasizing particularly the burdens on those physicians who, as members of a hospital board, might provide responsible awareness of patient problems.

J. Merrill Gibson, Jr, MD describes the successful treatment of a huge hamartomatous cyst of the liver.



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COMMENTARIES

Euphemisms, Paraphrasings and Other Late Summer Diversions

A major west coast medical school has recently renamed its plastic/reconstructive surgery unit, now calling it the Department of Esthetic Surgery. Some plastic surgery departments still cling to the older term but an expansion in their clinical responsibilities and a need to advance beyond older stereotypes have prevailed. Plastic surgery had been a surgical specialty devoted largely to cosmetic revamping and was rarely a specialty concerned with life-threatening illness or sometimes even illness per se. Since World War II, however, plastic surgery has broadened its mandate to include post-traumatic reconstruction, particularly of badly injured limbs. Appropriately, it changed its name to reconstructive surgery. Part of the current compulsion to change may be to distance itself from the older stereotype of plastic surgery and partly a need to describe the broader clinical implications of today's discipline; part to conform to reality, therefore, and part to present a name more pleasing, more appealing, more euphemistic.

We are, after all, a nation of euphemism-creators desperately seeking genteel locutions to blur the painful outlines of some unappealing reality. Take toilets, for example: While their functions have barely altered over the years, the names given to them certainly have been transformed. Awhile back they were called bathrooms, although few had bathing in mind when seeking them out in public places. Marginally accurate descriptors such as washroom or even powder room were then employed; now, finally, we call them comfort stations, which in a sense is reasonably accurate. Even the blunter term, latrine, is nothing more than a corruption of the Latin *lavatrina,* namely, a place to wash.

The word, crippled, is discarded as insensitive and has been displaced by the more compassionate term, disadvantaged. This too has been viewed disparagingly and is sometimes replaced by the still less accurate word, challenged.

Grave diggers became morticians. They in turn evolved into grief specialists. The corner saloons, the erstwhile targets of the hatchet-wielding temperance leader, Carrie Nation, transformed themselves into bars which in turn became cocktail lounges. Their ambience has changed but their dual purposes, namely liaison and intoxication, stubbornly remain. Euphemisms, eventually, become threadbare through rote usage; and ultimately they become patently transparent thus requiring either a new word to disguise the contours of truth - or the truth itself.

Name changes in the medical specialties may, at times, reflect a reorientation in clinical responsibility [e.g., general practice becoming family medicine.] And if a few branches of medicine have already boldly and courageously changed their names, why not the other healing disciplines ? Why, for example, does not radiology acknowledge its newly enhanced skills, many of which no longer rely upon X-rays ? A new name might be the Department of Insightful Imagery. And its partner in hospital-based medicine, surgical pathology, might consider being renamed the Department of Diagnostic Prescience while its pathological anatomy counterpart as the Department of Ultimate Inquiry. Endocrinology might be relabelled Glandular Equanimity; rheumatology, the Department of Articularly Challenged Medicine; neurology, the Department of Infracalvareal Analysis; and nephrology, the Department of Water Resource Management [to distinguish it from urology, the Department of Blessed Passage.] But these are benign pretensions, seeking neither to hide reality nor create major deception. Truer euphemisms, in Orwell's words, create language to give an appearance of solidity to pure wind. Consider, as examples of deceit, the following euphemistic phrases: fiscal parallelism for covert price-fixing; strategic misrepresentation, for diplomatic lying; or evading the issue for contraception.

Euphemisms can be mere preten-

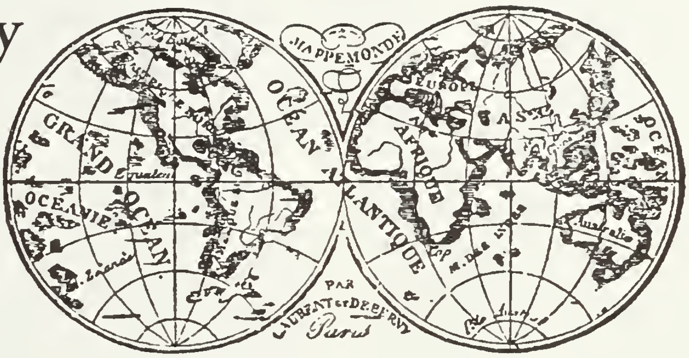
tious elegances but, for the most part, they are created to deflect the harshness, the indecorous qualities of a more pithy word or phrase. The more direct words are universally recognized but, by tacit consent, are rarely employed. The earthy language defining cloacal/coital structures and functions are certainly known to every child well before he learns the true obscenities of life such as genocide, racism and terrorism.

No paraphrase, however well-mannered, can be anything more than - or in some fashion independent of - the human function, structure or outcome that it had been designed to describe. And if a genteel Greco-Roman locution is indeed encouraged in polite society, it would seem that the avoidance of its vernacular equivalent becomes, at times, the greater obscenity.

A story is told of Harry Truman's early political career. He was speaking to a group of farmers and repeatedly talked about the barnyard as a placed filled with manure, manure, manure. A friend of Mrs. Truman whispered to her, "Why don't you teach Harry to say fertilizer ?" And Bess Truman responded, "Why Lord, Mathilda, it took me 30 years to train him to say manure !"

Stanley M. Aronson, MD

Lessons in Geography



Until recently all medicine - like all politics - was local. The territorial limits of a physician's concerns had been determined by the physical perimeter of his practice, by how far his horse-drawn buggy or sedan could take him in fulfilling his clinical tasks. The practitioner's perception of the ills of humankind was similarly parochial. While textbooks may have depicted exotic disorders, his daily experiences were confined to an earthbound range of disease possibilities. His horizon of clinical disorders went no further than that which he personally encountered in the villages within his catchment territory.

World War II broadened the global consciousness of this nation - and its physicians. Military imperatives brought many village-bred soldiers to alien lands; and in the peace that followed many more Americans traveled abroad for both commercial and recreational reasons. In a more interdependent and interconnected world, medicine necessarily transformed itself from a set of benevolent skills fulfilling local needs to an internationally oriented profession sensitive to a far greater range of diagnostic possibilities as well as public health interventions. By 1955, a physician practicing in Cranston might easily encounter malaria in a recently discharged army veteran, or some exotic enteric disease, requiring more than the usual over-the-counter medications, in a middle class civilian just returned from a vacation in the Caribbean. The textbook footnotes citing bizarre diseases were suddenly assuming relevance; and the insular village was becoming global.

The Korean War diminished America's isolation still further. Strange geographic words were now seeping into the collective vocabulary of the nation including alien names defining newly encountered illnesses. A hemorrhagic viral disease, once thought to be confined to a Korean river valley, has now spread to the United States but still carries its older name of Hantaan Fever.

The decade of the 1950's saw deliberate searches for pockets of new infectious disease, especially in subtropical and tropical regions. Large numbers of viral diseases were thus identified, each infection spread by an arthropod [mosquitoes, ticks, etc.] These pathogens were collectively called the arboviruses [arthropod-borne] and were named, generally, for the geographic sites where they were first isolated. From Africa, for example, Bunyamwera fever, Semliki Forest encephalitis, Bebaku fever and numerous others were added to the morbid roster of infectious diseases. From South America came Ilheus encephalitis, named after a small Brazilian port, and Paramaribo fever, named for a small Surinam community. It was observed, in passing, that some of these arboviruses preferentially attacked more rapidly growing cells including cancerous cells. Accordingly, in the 1950's, patients with leukemia and similar disorders were intentionally infected with these viruses in hopes that the cancer cells might be selectively destroyed. Beneficial responses were limited and this therapy is no longer employed.

The custom of calling illnesses by geographic site actually began well be-

fore World War II with such communicable diseases as Rocky Mountain Spotted Fever, St. Louis encephalitis, Japanese B encephalitis and Rift Valley Fever, to name but a few.

In recent years, as man and his settlements have encroached further upon the tropical rain forests especially of equatorial Africa, infections previously confined to monkeys have been transmitted to humans. And hitherto unknown villages such as Lassa, in Nigeria, and Ebola, in Zaire, have become immortalized as the names of grim new diseases.

Influenza is caused by an airborne virus which has the unpleasant characteristic of changing its genetic profile periodically such that a person recovering from last year's influenza carries no residual immunity when next year's mutated flu virus wanders into his community. Influenza is more than an occasional workplace inconvenience. It has probably killed more humans in the 20th century than any other single infectious agent. The threat is so great that a global surveillance system is in place to detect the first appearances of any new influenza strains. And when they do emerge, they are given geographic names such as Hong Kong, New Jersey, Japan or USSR strains.

The most egregious use of geographic names in identifying infectious diseases arose in the final decade of the 15th century when Spanish mariners brought back the spirochetes of syphilis from the New World. The ensuing epidemic was furthered particularly by numerous armies rampaging across central Europe. And as each nation encountered syphilis for the first time, it promptly named it after some neighboring country. Thus, much of southern Europe called it French pox, while the French - with Gallic modesty - called it Spanish pox.

Genesis says that in the beginning man was instructed to give names to all living creatures. But when it became necessary to name the invisible pathogens, problems arose forcing man to rely on such marginal qualities as the geographic sites where each disease was first confronted. There is some xenophobic arrogance in this tendency since it represents a way of proclaiming that our immediate vicinity would not now be threatened by the burden of pestilence were it not for the unhygienic permissiveness of neighboring nations who tolerated the existence and spread of such infections. On the other hand, the use of geographic names [whether it be Sindbis Fever from Africa or Lyme disease from Connecticut] reinforces our global interconnectedness. No place on earth is now more than 28 hours removed from our airports of entry. Truly, every village has become a piece of the continent, a part of the main. And suddenly, too, there is an additional reason to learn geography.

NORDAMERIKA.

Stanley M. Aronson, MD

Providing Health Care for the Russian-Speaking Patient

Anait Azarian, PhD, Robert J. Boland, MD and Vitali Skripchenko, PhD

Approximately 850,000 immigrants arrive in the US each year.[1] Many come from the former Soviet Union: in 1993, former Soviets were fifth among legal immigrants, and they were the most common refugees. In 1995, of 110,000 legal refugees, 48,000 were from Eastern Europe and the former USSR.[2]

Rhode Island has not been immune to this influx. The 1990 US Census identified 897 persons over age 5 in Rhode Island who considered Russian the primary language spoken at home. [3]

It is the authors' experience that these patients offer special challenges to the health care provider. Differences in language, background, and culture separate health care providers from their Russian-speaking patients. This article is a first attempt to supply clinicians with relevant information and recommendations.

BACKGROUND

Americans often group Russian-speaking immigrants together as "Russians." This grouping includes people of Jewish, Armenian, Russian, Ukrainian, Byelorussian, and other heritages. The only thing these different groups have in common is their fluency in Russian (thus, we will refer to this group as "Russian-speaking"). The next sections will consider some historical and cultural aspects of Russian-speaking immigrants.

HISTORICAL ASPECTS

Almost all Russian-speaking people in RI have arrived since 1970. They are quite different from the earlier waves of immigrants from Czarist Russia and the Ottoman Empire (Turkey) at the turn of the century. Russian-speaking immigrants have lived their entire lives under a Communist regime, which has imposed a distinct imprint on them.

Until Gorbachev's *perestroika* of the late 1980's, ethnic emigration from the USSR was sanctioned only on the grounds of family reunification. Even then, immigration was often refused for reasons of "security." Applicants had to pay reimbursements for their diplomas and degrees. They also had to obtain permission from parents, employers, the local Communist party and administrative authorities. This could lead to public denunciation of the emigre. Thus, most potential emigres were strongly discouraged by this process.

If a visa was granted, the route from USSR to USA was long and indirect: through Vienna or Rome, where the immigrants were likely to remain for months waiting for the necessary immigration papers from the US.

This situation has improved only in the last few years. Applicants experience less societal pressure, and they can fly directly from Moscow to the US. Many people from the former Soviet republics now apply for permanent alien residency ("green card") within the U.S. after arriving here as tourists, students, or businessmen.

SOVIET JEWS

Emigration was particularly difficult for Soviet Jews, who were historically the most oppressed ethnic minority. It is not surprising that anti-Semitism represents the most common reason given by Russian-speaking Jews for emigrating to the US.[4]

Former-Soviet Jews are often highly educated, and many are artists, teachers and professionals. They often differ, however, from American Jews in that they may be less religious.. They often emigrated from major metropolitan areas, such as Moscow, Kiev, Odessa, or Minsk. Many Jewish refugees also came to Rhode Island from the Byelorussian town of Gomel, following the Chernobyl nuclear station disaster in 1986. Their primary—and frequently, only—language is Russian. Many now live in Providence and Pawtucket.

Adaptation to the US is somewhat eased with the help of the Hebrew Immigrant Aid Society (HIAS) and other Jewish organizations. In Rhode Island, Jewish immigrants can take English classes, vocational courses and social/cultural programs at the Jewish Community Center.

ABBREVIATIONS USED

HIAS	Hebrew Immigrant Aid Society

ARMENIANS

Former-Soviet Armenians in Rhode Island consist of two distinct groups: immigrants from the Armenian Soviet Republic, and refugees from Azerbaijan. The former speak Armenian, though many are fluent in Russian. Many experienced the 1988 earthquake in North-East Armenia that took the lives of 55,000 people.

Most Armenians did not experience the ethnic oppression common to former-Soviet Jews. The exception to this is in Azerbaijan, where ethnic discomfort culminated in the massacre of Armenians from 1988 to 1990. About 250,000 Armenians escaped to other republics of the USSR; from there some came to the US. About 50 families arrived as refugees to Rhode Island. They generally speak Russian, although some are fluent in Azerbajani or Armenian dialects.

Among Soviet Armenians are people with university degrees and skillful artisans. In Rhode Island they met a prosperous Armenian community of about 10,000 who came, much earlier, from Turkey, Syria, Lebanon, and Iran. These established American-Armenians often do not speak Armenian, or speak different dialects. As with former-Soviet Jews, former-Soviet Armenians often do not have the religious affiliation of their American counterparts. They may attend the three Armenian churches in Rhode Island for social events. They live mostly in Cranston, Providence, Warwick, and North Providence.

Russians, Ukrainians and Byelorussians

Many Russians, Ukrainians, and Byelorussians came to RI for religious reasons. Others came to accompany their Jewish or Armenian spouses; they often have no religious orientation, or they are regular followers of the Russian Orthodox Church. There is only one Ukrainian church in Rhode Island, located in Woonsocket.

These groups—particularly Byelorussians—have almost completely lost their ability to speak their native language, due to the longtime promotion of the Russian language in their republics (known as "Russification"). They are fewer than the other Russian-speaking immigrants, and live throughout Rhode Island with no distinct locus.

Adoptees

The children from former-Soviet orphanages who were adopted by Rhode Island families comprise an additional population of Russian-speaking immigrants. Though currently small in number, it is expected that their number will increase. It is also expected that they will have special educational and health needs; however, the present article will primary deal with adult patients and their families.

Health Care in the Former Soviet Union

The term "health care" is itself alien to the Russian-speaking immigrant, where a "medical system" was more the purview of Soviet clinics and hospitals. Though talented individuals existed, the health care system was oriented toward bureaucratic administration and self-preservation. For the Soviet patient, obtaining care, medications or hospitalization was a constant challenge that often required favors and bribes. Given this experience, it is easy to understand why, despite our best intentions, the Soviet patient may view the American health care provider with suspicion.

As American clinicians, we focus on a patient's individual abilities and autonomies. Our Russian-speaking patients, however, came from a society that stressed the sacrifice of personal goals for the collective good of the family, community or nation. Treatment is likely to be succcessful, for example, if the clinician engages the family as well as the patient and presents goals in terms of benefits to the entire family.

Mental Health Care in the Former Soviet Union

Russian-speaking patients come from a country where the mental health of its citizens was of little concern to health care institutions. Often, health care workers in the Soviet Union did not distinguish between psychological and physical symptoms. Greater value was placed on somatic rather than emotional complaints. Psychiatry was primarily inpatient-based, and often functioned as an agent of the state to remove dissidents. Clinical psychology or psychotherapy did not exist in the former Soviet Union—it was not accepted that there could be psychosocial problems in a "utopian" society.

Immigration as a Psychosocial Stressor

There is a saying among the Soviet immigrants: Every newcomer to the US should bring with him two stones. During the first two years, he will hit his head with one stone saying, "Why did I come to this country?" The second one he will use afterwards, saying "Why did I come here so late?"

Migration can cause, precipitate, and exacerbate both physical and mental disorders. This section will describe some psychosocial stresses facing the Russian-speaking immigrant.

Communication

The most obvious difficulty is language.[5] Although many Russian-speaking immigrants may have studied English in school, the training was usually minimal. Thus, compared with other European immigrants, Russian-speaking immigrants tend to be much less fluent in English.[6] As with most people learning a new language, their reading abilities are better than their writing, and their writing abilities are better than their verbal skills.

Financial Stressors

After a few years in the US, most Russian-speaking immigrants can adjust to their new environment, and they are proving to be a useful investment for the host country.[6] However, during their initial years in a new country, they must confront the fact that they have to begin their careers anew. This can be especially painful for the professional. They may be unable to accept this reality, and cling "compulsively" to their past identity.[7]

FAMILIAL STRESSORS

Russian-speaking people can have close family ties. Armenians generally maintain traditional extended families, Russians often have only nuclear family ties, and Russian-speaking Jewish immigrants are somewhere between.

In the Soviet Union, children were expected to treat their parent's word as law. Now, with surprising rapidity, the children may find themselves the only medium through which their parents can communicate. Thus, the child or adolescent begins to feel a new sense of power over the parents. This is compounded by exposure to American culture: differences in dress, food, language, and behavior. The child may feel ashamed of family traditions (for example, one Russian immigrant recalled being asked by her children not to speak Russian when the children's friends were there). The immigrant children may feel isolated from their parents. The parents may, in return, wish to enforce their rights and authority. The sequelae of such sudden role changes can lead to family instability.

ACCULTURATION

Following these problems with adjustment is the opposite stress—the fear of acculturation. This can particularly involve parents' fears over the Americanization of their children. Since the Russian-speaking population is small, there is little impetus to maintain traditions, as there might be in larger cities.

For the immigrant, these different stressors come simultaneously, and interact in significant ways. The immigrant whose lack of English prevents his working may stay at home, and not associate with non Russian-speaking people. As a result, their English is unlikely to improve much over time. While staying home, their children are going to American schools. The children's growing English gives them a tremendous advantage over their parents, and this changes their relationship.

PSYCHOLOGICAL ISSUES WITH RUSSIAN-SPEAKING IMMIGRANTS

Common sense, and clinical observations, suggest that immigrant or refugee status is associated with a higher frequency of psychiatric conditions.[8,9,10] The act of immigration causes a level of distress and trauma, which may precipitate psychopathology in a person so predisposed.

For the immigrant with a premorbid psychiatric history, any clinical records that accompany them are likely to be confusing. In the Soviet system, there was no manual akin to our Diagnostic and Statistical Manual-IV. Thus, diagnoses are often idiosyncratic. Many syndromes went unrecognized, such as Attention Deficit Disorder or Post Traumatic Stress Disorder. When diagnoses are given, they often have a pseudoneurological quality to them, reflecting the cultural preference for somatic etiologies.

It is unclear whether major psychiatric disorders are more prevalent among immigrants than the general population.[11] There is some evidence to suggest that schizophrenia can occur with greater prevalence in immigrants.[12,13] Regardless, it is certain that these disorders are a challenge to any clinician.

Major depression may be the most common disorder among Russian-speaking newcomers. It may occur more frequently during the first two difficult years; however, studies in other populations have shown persistence of depression long after resettlement.[14,15] Often, the only clue to this disorder may be the patient's complaint of multiple vague somatic complaints.

Other disorders, such as adjustment and post-traumatic stress disorders, may also be common, given the number of aforementioned stressors immigrants may have experienced.

ISSUES FOR THE HEALTH CARE PROVIDER

THE DOCTOR-PATIENT RELATIONSHIP

"Hi, nice to meet you...how are you today?" The man looks uncomfortable. He scowls and mutters to the interpreter in Russian, "Who is this fool?" Later, the interpreter explains: "He thought you were a ninny because you were too friendly. Next time, try wearing a white coat and acting more formal." [16]

Some Russian-speaking patients are accustomed to a more formal relationship between doctor and patient. They may view the relative informality of American providers as unprofessional. The result may be a misuse of the system by the Soviet patient, in a manner more appropriate to the Soviet style of care.

FINANCIAL ISSUES

In the former Soviet Union, medical services were free. Thus, when being told that they must make co-payments to a physician, they may become discouraged by what appears as an unfair demand. They may discontinue further treatment, even though the specific costs are not a financial burden to them. They simply cannot comprehend this attribute of American health care.

DEVELOPING RAPPORT

In an effort to improve compliance, the clinician began explaining, in very simple terms, the pharmacological actions of the medications he was prescribing. The patient suddenly brightened, laughed and talked with the interpreter. It soon became evident that the patient had been a research pharmacologist in Russia, who knew a good deal more than the clinician about these medications, and that the patient's noncompliance was not related to ignorance, but rather intellectual disagreements about the proper use of these medications.

In developing rapport, it is particularly important for the clinician to make use of the Russian-speaking patient's strengths. The patients are often highly educated. They can grasp very complicated medical information, if it is clearly explained. With a better understanding of the goals and reasoning for treatment, one can expect better compliance.

ALTERNATIVE TREATMENTS

The patient was asked to describe her medications. She presented the doctor with a list of medications prescribed by her internist. It was only several sessions later that she brought some pills she said had been using for sleep. The packaging was in Russian. The clinician assumed that she had brought these pills with her from Russia, and advised her not to use them. Several months later, she returned with another Russian medication she was using for sleep. When asked, she explained that there was a pharmacy in Rhode Island which can obtain Russian medications.

Though many clinicians are unaware, there exists an alternative system of care, consisting of Russian healers and medication. This system is not illegal; however, there is little quality control over the system.

As with alternative medicine in general , the clinician must walk a difficult line. Though it is usually preferable to remain open minded, the clinician is also in the role of protecting the patient from exploitation. As shown above, a first step is to obtain information, as most patients—Russian or otherwise—may assume that the doctor is only interested in discussing traditional medical treatment.

THE FAMILY IN TREATMENT

It is important to understand the value placed on family relationships. Though our natural inclination is to interview patients alone, out of concern for confidentiality, proper time and respect should be given to family members as well. Ultimately, engaging the entire family in treatment is crucial to fostering a good doctor-patient relationship.

THE ROLE OF THE INTERPRETER

Often, hospitals rely on any person with bilingual understanding. Alternately, family members are used as interpreters. The cross-cultural literature, however, shows the importance of sophisticated interpreters, or so-called "national consultants."[17,18,19] Such interpreters should be able to not only translate the verbal meaning of a patient's communication, but also convey non-literal and nonverbal communications. They should be attuned to normal behavior and attitudes in a patient's culture. Furthermore, they may be best suited to resolve misunderstandings between the patient and the health care system.

As the Russian-speaking population is, in part, a small community, it is not unusual that the interpreter and patient will know, or know of, each other. Our need for easily available translation must be weighed against concerns for confidentiality.

MENTAL HEALTH ISSUES

For the mental health clinician, we have already noted the Russian-speaking tendency to value "scientific" or "practical" solutions to psychiatric problems. One can expect that the Russian patient will be likely to interpret emotional problems as physical, and present to a primary care doctor for treatment. It is the primary care doctor, therefore, who will be on the "front line" to screen for psychiatric symptoms. This can be particularly difficult if they are expressed somatically—particularly when done so through another language and culture. The result of proper recognition of the problems, however, can mean the avoidance of needless tests, procedures and treatments.

FUTURE DIRECTIONS

Currently, our system of physical and mental health care does not really meet the needs of Russian-speaking patients. Such patients seek out health care at most of the available sites in Rhode Island. Since the care is so spread out, it is not practical for most of these sites to offer special accommodations for Russian-speaking patients. Thus, though Russian interpretation is usually available, there is little else to help the patient's adjustment into the American health care system.

A specific program, targeting Russian-speaking patients, could be developed, either at a single site, or as part of a consortium. Such a team could combine case management, bilingual interpretation, social services, primary and mental health care. Familiar with the Russian-speaking patients' historic and cultural background, this team could better recognize the potential pitfalls to appropriate health care utilization, and provide more comprehensive, and presumably more effective treatment.

SUMMARY AND RECOMMENDATIONS

On examination, the patient was asked about use of medications. She explained that she had been put on an ever increasing number of antihypertensive medications, all in an effort to control what appeared to be an uncontrollably malignant hypertension. The clinician asked her to describe her use of the medication. At first she replied, "I take it the way they said." When asked more specifically, she revealed a very erratic regimen, in which some days she took more than prescribed, some days less, and some days not at all. She said this depended upon how she "felt" her blood pressure was on that particular day—evidently referring to a headache. She added that a medication she borrowed from her sister seems to be more helpful.

Although the clinician dealing with the Russian-speaking patient may lack cultural expertise, that clinician can be very helpful if he or she maintains an open and flexible approach.

The initial visit should be unhurried, to allow more time for the building of rapport. Sufficient time should be spent in explaining the major principles of treatment, and the key points of the clinician's services. Written or illustrated explanations can help bridge the language gap.

Clearly, there is no "cookbook" of approaches that work for certain groups of patients. Individual flexibility is the most valuable tool in building rapport. However, it has been noted that at least some Russian-speaking patients may prefer a more formal approach.

Others will benefit from careful explanations of the reasoning behind treatment. Simply asking a patient to take a medication may not be enough—stressing the importance of regular administration, as well as carefully explaining the rationale for treatment may be more helpful.

If using an interpreter, all three parties should be seated in an equilateral triangle, thus, able to observe each other. This approach—the "communication model"—allows the clinician to observe both the patient and the interpreter and to attend to their nonverbal behavior. Furthermore, it discourages the use of interpreters as merely "word unscramblers" and acknowledges their inevitably active role in the discourse.

As American clinicians, we focus on a patient's individual abilities and autonomy. Our Russian-speaking patients, however, came from a society that stressed the sacrifice of personal goals for the collective good of the family, community or nation. Treatment is more likely to be successful, for example, if the clinician engages the family as well as the patient, and presents goals in terms of benefits to the entire family.

We have found treating Russian-speaking patients to be a rewarding experience. This is a group of patients in great need of competent medical care, who have been unable to obtain it for most of their lives. Many chronic medical conditions have gone unrecognized or neglected. Thus, there is much work to be done. Furthermore, they represent a group that, with a proper doctor-patient relationship, is well suited to benefit from good medical care.

The clinician who shows interest in this population will find no lack of opportunity. Russian-speaking patients have tended to rely on personal networks and recommendations over other forms of referral. Thus, a single referral of a Russian-speaking patient is likely to develop into a greater relationship with a rewarding community of persons.

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Hemoptysis In Sarcoidosis: A Case Report

Annie Lin Parker, MD, Ellen M. Clarke, MD, and Sharon Rounds, MD

ABBREVIATIONS USED

PPD	Purified protein derivative [of tuberculin]

Pulmonary involvement in sarcoidosis is common. Up to 90% of patients have abnormal chest x-rays and 50% of patients experience symptoms localized to the chest.[1] However, hemoptysis only occurs in 1-6% of sarcoid patients.[2] When hemoptysis does occur, it is usually a sign of superinfection. More rarely, it may result from endobronchial lesions or mucosal irritation from chronic cough. Massive hemoptysis is rarely due to pulmonary sarcoidosis alone. Efforts should be made to evaluate for a second disease process in sarcoid patients with hemoptysis.

CASE REPORT

The patient was a 36 year-old white male who was admitted to our institution with persistent cough and hemoptysis. Patient was evaluated in the emergency room the month before admission with a complaint of pleuritic chest pain. Chest radiograph at that time was remarkable for left upper lobe infiltrate and mediastinal widening. Patient was given a two week coures of penicillin without improvement. On admission, patient had stable vital signs and was afebrile. Auscultation of the lungs revealed scattered rhonchi. The fingers were clubbed. The rest of the physical examination was unremarkable. Laboratory data were only significant for hemoglobin of 11.5 and hematocrit of 34. The chest radiograph showed persistent left upper lobe infiltrate and a wide mediastinum (Figure 1). Computerized tomography of the chest revealed left upper lobe infiltrate with adenopathy and an anterior mediastinal mass (Figure 2). PPD was placed and was negative at 48 hours. Bronchoscopy was performed and active bleeding from the left upper lobe orifice was noted. There were no endobronchial lesions. Cultures of bronchial washings for bacteria, fungi, and mycobacteria were negative. Cytologic examination of bronchial washings revealed no malignant cells. During this hospitalization, his hemoglobin decreased to 6.4, which was partially attributed to a bleeding duodenal ulcer seen by gastroduodenoscopy. He then underwent mediastinoscopy and biopsy of the anterior mediastinal mass which showed non-caseating granulomas consistent with the diagnosis of sarcoidosis (Figure 3). The hemoglobin and hematocrit stabilized, and the patient was discharged from the hospital. Two weeks later, the patient was readmitted with dyspnea, weakness and hemoptysis. Hemoglobin on admission was 6.0, and the patient required multiple transfusions for persistent hemoptysis. Because the degree of hemoptysis

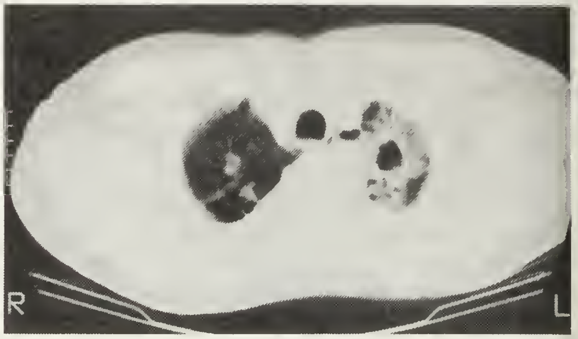

Figure 2. Panel A
Chest computed tomogram shows bilateral infiltrates, cystic changes, and a thick walled cavity in the left upper lobe.

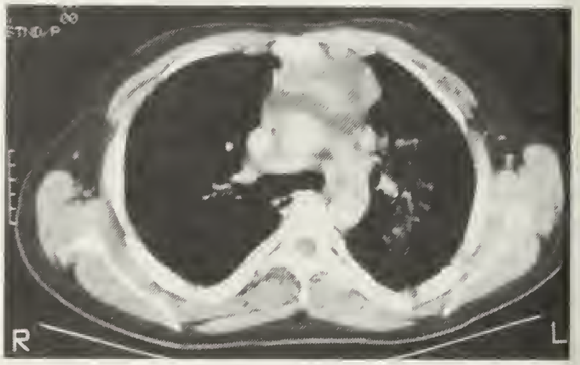

Figure 2. Panel B
A large inhomogeneous anterior mediastinal mass is present.

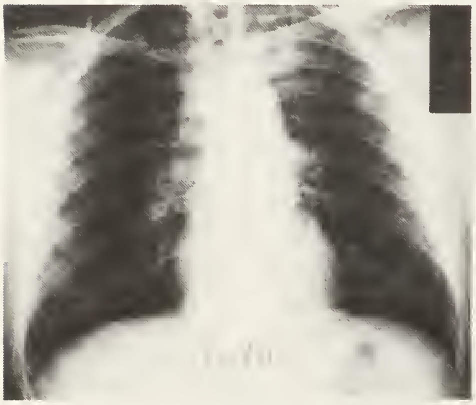

Figure 1.
The chest roentgenoram shows a left upper lobe infiltrate and widened superior mediastinum.

> *... because hemoptysis is unusual in sarcoidosis in the absence of infection, patients with sarcoidosis who develop hemoptysis should be evaluated for a second disease process.*

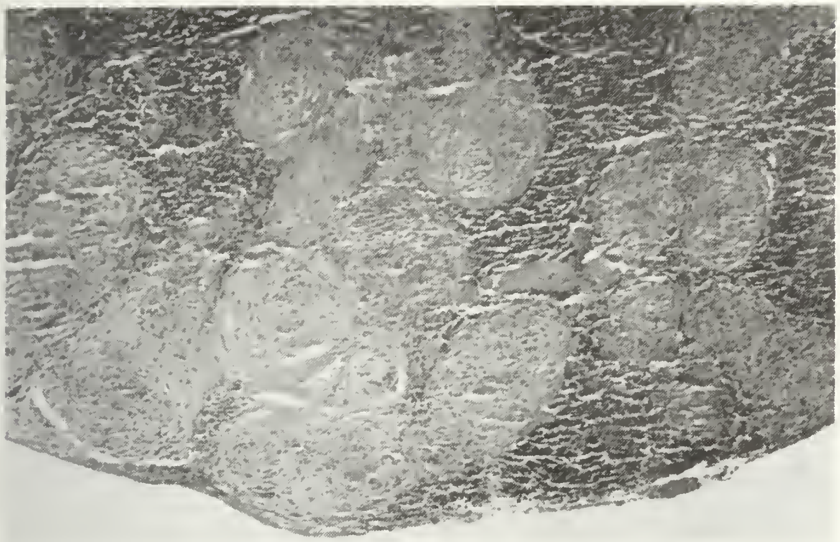

Figure 3.
Biopsy of the anterior mediastinal mass reveals a lymph node infiltrated with numerous, well-formed, non-caseating granulomas. (Hematoxylin and eosin, X 92)

was unusual for sarcoidosis, bronchoscopy was repeated and cytological examination of bronchial washings revealed non-small cell lung carcinoma. Due to persistent hemoptysis, surgical resection was recommended. At thoracotomy, there were multiple small, hard, gray nodules throughout the lung parenchyma. Biopsy of the nodules revealed non-caseating granulomas. Biopsy of the mediastinal mass revealed giant cell carcinoma. Left pneumonectomy and resection of the mass were performed. The patient's postoperative course was complicated by adult respiratory distress syndrome, episodes of bradycardia and complete heart block, requiring transvenous pacemaker placement. On the 24th postoperative day patient suffered a cardiac arrest and expired.

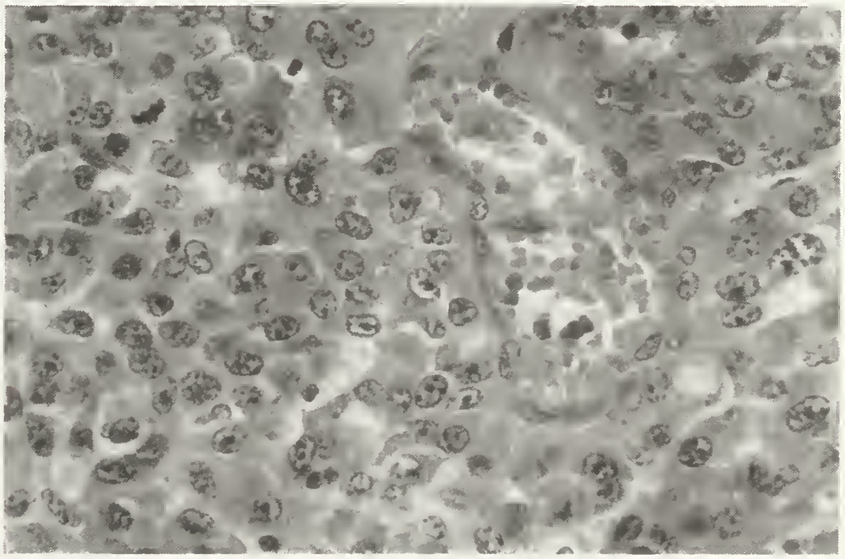

Figure 5
Histologic section of the lung parenchyma adjacent to the upper lobe cystic space shows vascularized malignancy with large, neoplastic cells with prominent nucleoli. (Hematoxylin and eosin, X 200)

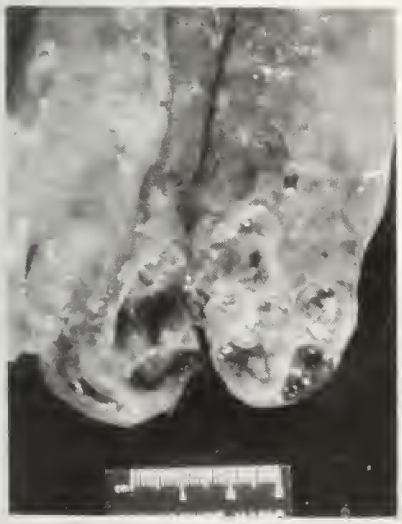

Figure 4
The bisected, surgically removed left upper lobe shows hemorrhage and apical cavitation.

The surgically removed left lung had a cystic cavity in the upper lobe (Figure 4) with malignant cells in the cavity wall and adjacent lung parenchyma (Figure 5). The mediastinal mass was necrotic and cystic, filled with hemorrhagic fluid. The histologic characteristics of both the lung and the mediastinal mass were conssitent with giant cell carcinoma. Adjacent to the left upper lobe cavity and throughout the upper lobe parenchyma were multiple granulomas, some of which appeared fibrosed. At autopsy, there were metastatic foci of carcinoma in the mediastinum, peri-gastric lymph nodes, pleura, and pericardium. Granulomas were also found in the mediastinal lymph nodes, pericardium, and the right lung.

Discussion

Sarcoidosis is a multisystem granulomatous disorder of unknown etiology. Pulmonary involvement in sarcoidosis is common. Up to 90% of patients have abnormal chest x-rays and about 50% experience symptoms such as dyspnea, nonproductive cough, and chest pain.[1] Hemoptysis is uncommon in the course of chronic sarcoidosis, and rare as the presenting symptom of the disease. Chang and coworkers studied 433 patients with sarcoidosis, and 25 patients (6%) were found to have hemoptysis. Of the 25 patients with hemoptysis, 19 had mild hemoptysis, 4 had moderate, and only 2 had massive hemoptysis.[2] When hemoptysis does occur, it may be due to several possible causes: 1) invasion of pulmonary vessels by granulomas; 2) mucosal irritation from persistent cough caused by endobronchial sarcoid lesions; 3) bronchiectatic changes inducted by sarcoidosis; 4) infectious complications of sarcoidosis, such as aspergiloma in cystic spaces complicating chronic fibrosing pulmonary sarcoidosis.[3]

Lung cancer was an unexpected finding in this young nonsmoker. The association of malignant neoplasms and sarcoidosis is controversial. Brincker and Wilbek reported that of 2544 patients with respiratory sarcoidosis registered in the Danish Institute of Clinical Epidemiology, 48 patients developed a malignant tumor in a 10-year follow-up. Only 33.8 cases of cancer were expected if sarcoidosis patients had had the same rates as the general population. The authors proposed that the statistically significant increase in cancer incidence may have resulted from immunological deficiencies in patients with sarcoidosis.[4] However, when Romer reviewed the same data, he suggested that the number of malignancies in the patients with sarcoidosis was not more than would be expected by chance alone.[5] Pathologically, it is well known that non-necrotizing granulomas can be found in association with a variety of neoplasms. Granulomas may be observed in lymph nodes draining the site of malignancy, in the primary tumor itself, and even in non-regional tissues. Such tumor-related histologic changes are termed "sarcoid reactions" and are not indicative of systemic sarcoidosis. Overall, sarcoid reactions occur in 4.4% of carcinomas, in 13.8% of Hodgkin's disease, and in 7.3% of non-Hodgkin's lymphomas. [6] Sarcoid reactions in lymph nodes not involved with tumor are not likely to be a result of direct interaction between tumor cells and lymph node tissue. More likely, sarcoid reactions are caused by antigenic factors derived from the tumor cells, eliciting an immunological hypersensitivity reaction leading to the formation of granulomas.[6] Occasionally, sarcoid reactions may be so extensive that it is diffciult to distinguish between tumor-related sarcoid reactions and true systemic sarcoidosis. Because of the well formed histologic appearance of the granulomas, we believe that our patient had concurrent sarcoidosis and lung cancer. However, the possibility that he actually had lung cancer with extensive sarcoid reaction can not be completely excluded.

Finally, because hemoptysis is unusual in sarcoidosis in the absence of infection, patients with sarcoidosis who develop hemoptysis should be evaluated for a second disease process.

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Does Antecedent Splenectomy Alter the Course of HIV Infection?

Aijaz Ahmed, MD, Erik N. Watson, MD, and Charles C.J. Carpenter, MD

Splenectomy increases the incidence and severity of specific bacterial infections caused by encapsulated microorganisms, especially Streptococcus pneumoniae.[1] HIV infection is associated with increased incidence and severity of pneumococcal infections[2], due to the poor immunological response to polysaccharide antigens.[3] Therefore, persons with both HIV infection and splenectomy may be more susceptible to severe pneumococcal infections.[4] In our experience, with over 800 persons with HIV infection, we have identified three individuals who had splenectomy from 7 to 9 years before HIV infection was documented. The documentation of HIV infection was made on voluntary testing on admission to the Rhode Island Adult Correctional Institution (ACI). All hospitalizations and all recognized infections which occurred after splenectomy in each of the individuals were tabulated and analyzed. None of the patients showed any clinical manifestations which appear to be the consequence of HIV infection. None of the individuals received antiretroviral therapy. Two persons (a male and a female) showed a slight increase in CD4 count over a 5 to 7 year period of observation. The third (a female) has shown a gradual fall in CD4 count over a 7 year period. These observations are inconclusive, with so small a data base, but lead us to suggest a systematic evaluation of the possible effect of antecedent splenectomy on the response to HIV infection.

ABBREVIATIONS USED

ACI	Adult Correctional Institution
AIDS	Acquired immune deficiency syndrome
HIV	Human immunodeficiency virus
IDUs	Intravenous drug users
SIV	Simian immunodeficiency virus

OBSERVATIONS

Because a large proportion of our patients with HIV infection (over 75% of men and 48% of women), are former intravenous drug users (IDUs), many have engaged in high-risk behavior resulting in abdominal trauma. In review of our records we have found three former IDUs who had unequivocal documentation (operative report and onset of clinical features) of post-traumatic splenectomy prior to infection by the HIV. We have evaluated the clinical courses of these individuals; the data suggest that antecedent splenectomy may favorably influence the course of HIV infection.

...most reports to date suggest that splenectomy neither accelerates nor retards the progressive immunodeficiency in the HIV infected individual.

All 3 patients were followed for at least five years by physicians participating in The Miriam Hospital Immunology Center, a component of the Brown University AIDS Program; and all had periodic clinical evaluations and CD4 lymphocyte determinations. All 3 patients were incarcerated at least once during the period of observation in the Rhode Island Adult Correctional Institution (ACI). Incarceration facilitated follow-up, since medical care for HIV-infected individuals in ACI is provided by physicians from the Miriam Immunology Center.

The rate of change of CD4 over the period of observation were calculated in each individual (Table 1). Two of the three patients showed no decrease in CD4 count during 5 to 7 years of observation. One individual demonstrated a mean fall in CD4 count of 48 cells/year, a rate which approximates the average rate observed in North American women with HIV infection.[5] None of the patients have shown any clinical consequences of HIV infection, and none of the individuals have received antiretroviral therapy.

DISCUSSION

During the early course of the HIV epidemic, a number of persons with thrombocytopenia associated with unrecognized HIV infection underwent splenectomy as a therapeutic maneuver. Subsequent observations have suggested that splenectomy did not have an adverse effect on the course of HIV infection.[6,7] Splenectomy is still considered by some clinicians to be a reasonable treatment for refractory thrombocytopenia in persons with HIV infection.[6,7] Although one report indicated that the immediate effect of splenectomy was to increase the CD4 count in peripheral blood of individuals with HIV infection, most reports to date suggest that splenectomy neither accelerates nor retards the progressive immunodeficiency in the HIV infected individual.[6]

The recent observation by Narayan that antecedent splenectomy renders macaques less susceptible to

	Sex	Age at splenectomy (years)	Age at HIV diagnosis (years)	CD4 count at HIV diagnosis (cells/ul)	Most recent CD4 count (cells/year)	Observed change in CD4 count (cells/ul/year)
Patient 1	Female	30	39	700	780	+10
Patient 2	Male	26	33	600	640	+1
Patient 3	Female	19	27	700	380	-48

Table 1: Rate of change in CD4 lymphocyte counts over 5 to 7 years in three HIV-1 seropositive individuals with antecedent (> 7 years before HIV infection) post-traumatic splenectomy.

intravenous infection by SIV suggests that prior splenectomy may interfere with the establishment of chronic SIV infection in this animal model, which bears many clinical and laboratory similarities to human HIV infection.[8] Furthermore, reports from a number of investigators suggest that the efficient filtering and trapping of HIV by the follicular dendritic network in the spleen and other lymphatic tissue may facilitate the infection of associated CD4 positive T cells, and therefore serve as a reservoir in which HIV replication and CD4 lymphocyte infection may occur rapidly in the earlier asymptomatic phases of HIV infection in the human.[9,10,11,12,13]

Both the work in the macaque model of SIV infection and observation in human HIV infection are consistent with the concept that the intact spleen plays a facilitating role in the early phases of HIV infection. The case reports presented here are consistent with this hypothesis. In present cases, no progression of immunodeficiency was observed in over 5 to 7 years in 2 of 3 patients.

The spleen does not appear to serve a unique role in early HIV infection, since essentially the same process of virus trapping occurs in other lymphatic tissues. It is therefore likely that lack of progression in two of the three patients indicates a delay, rather than absence of progression of HIV infection, an issue which will be solved only by further longitudinal follow-up. These data, however, if confirmed by studies of larger numbers of HIV-infected patients with prior splenectomy, are consistent with the possibility that prior splenectomy favorably alters the course of individuals infected by HIV.

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The Detection of Translocations Using Chromosome Painting for Monitoring Exposure to Potential Genotoxicants

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The effects of genotoxic agents, including certain pharmaceutic compounds, can be acute or long-term. The evaluation of toxic effects in human populations after exposure to potential genotoxicants is often limited to the evidence of an acute response. Long-term effects are usually inferred by extrapolation.

Dicentrics have traditionally been used as an endpoint to measure the genotoxic effects of potential hazardous agents on chromosomes in both dividing somatic and germ cells. However, dicentrics are not stable with time, probably due to the occurrence of breakage-fusion-bridge cycles.[1] Depending on the dose, a proportionate decrease in the relative frequency of dicentrics was observed, suggesting that cells with dicentrics are eliminated from the circulation with time. [2-5]

A more suitable assay is the detection of translocations via fluorescent *in situ* hybridization (FISH) using chromosome painting.[6]

Materials and Methods

Cell Culture and Harvesting of Metaphases

The procedure for culture and harvest for genotoxicology testing is given in detail in Mark et al.[7,8]. Slides for chromosome painting can be prepared using routine cytogenetic procedures. Briefly, peripheral blood lymphocytes are cultured for 72 hours at 37°C in the presence of phytohemagglutinin[9], a mitogen extracted from kidney beans. Harvesting of short-term lymphocyte culture is performed according to a modification of the conventional method[10], using Colcemid (deacetylmethylcolchicine) as the metaphase arrestant, 0.075 M KCl as the hypotonic agent, and three parts of methanol to one part of glacial acetic acid as the fixative.

Fluorescent In Situ Hybridization (FISH)

For the detection of translocations, FISH using a collection of probes derived from various regions of entire chromosomes is the technique of choice. Directly labeled ("whole chromosome painting") probes are used (Gibco BRL/Life Technologies, Inc., Gaithersburg, MD). For simultaneous chromosome painting of two different pairs of chromosomes, two different fluorochromes are used in addition to the counterstain. Both Spectrum Orange and Spectrum Green (Gibco BRL/Life Technologies, Inc., Gaithersburg, MD) give brilliantly painted chromosomes in a blue DAPI background.

> *... fluorescent in situ hybridization using chromosome painting probes can often yield additional information that is otherwise unobtainable by the traditional chromosome aberration assay alone.*

Briefly, the first day of the procedure includes denaturation of the slides in a formamide solution at 70°C, wash in an ethanol series at room temperature, air-drying of slides and application of heat-denatured probes. Overnight hybridization is at 37°C in a moist chamber (Isolab, Inc., Akron, OH; see Mark [11] for details). On the second day, after coverslips are removed, slides are post-washed in formamide solutions at 45°C and air-dried. The final counter-staining steps include the application of DAPI counterstain.

Abbreviations Used

DAPI	4,6 - diamidino-2-phenylindole
FISH	Flurorescent in situ hybridization

Signals are detected by following the manufacturer's instructions exactly and with the aid of special microscope filters and a Zeiss epifluorescence microscope as described previously[6]. Metaphases are viewed using the 40X and 100X objectives and photographed with a Zeiss epifluorescence photomicroscope using Ektachrome ASA 400 or 200 color film.

Discussion

Structural chromosomal rearrangements resulting from genetic damage include translocations, paracentric and pericentric inversions, tandem and inverted duplications, terminal and interstitial deletions, isochromosome formation, rings, markers, acentric fragments and complex rearrangements. Of these, dicentrics have traditionally been used as an endpoint for measuring damage to chromosomes. For the most part, dicentrics have been scored using human peripheral blood lymphocytes.[12-16]

The use of dicentrics as an assay of genotoxicity, however, suffers from the drawback that the frequency of cells containing dicentrics decreases with time post exposure[2-4], presumably due to the resultant breakage-fusion-bridge cycles. For example, dicentrics cannot

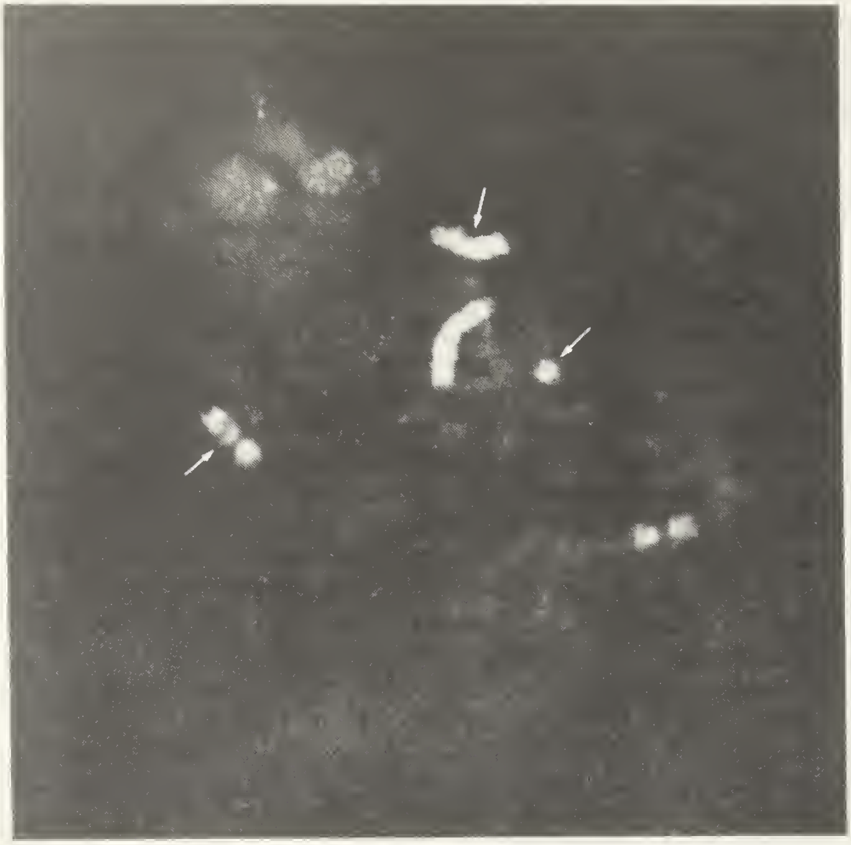

Figure 1. Fluorescent *in situ* hybridization illustrating the use of chromosome painting probes for the detection of translocations. The three white arrows point to derivative (rearranged) chromosomes detected by chromosome painting. The two other painted chromosomes are non-rearranged chromosomes, in this case, chromosomes 2 and 9. In the original photograph, the chromosome 2 appeared green, the chromosome 9 appeared red, and the rest of the chromosomes in the metaphase spread appeared blue.

be used in the dosimetry of persons chronically exposed to radiation or in persons exposed months or even years previously.[17-19]

Translocations are found, however, to be stable with time post-exposure [2,12,20], presumably due to the capping of chromosome/chromatid ends. Therefore, translocations should be a useful indicator of genetic damage even long after the exposure to chemical or physical genotoxicants, or as an indicator of damage accumulated during chronic exposures. Accurate biodosimetry is important both immediately after exposure and at longer intervals after exposure. The former can be used as a guide for medical treatment, the latter for assessing the health consequences in exposed individuals.

Experience in this laboratory has demonstrated that the fluorescent *in situ* hybridization technique is useful for a number of applications.[6] For genotoxicology testing, alpha-satellite probes can be used to detect chromosome aneuploidy as a measure of induced chromosome nondisjunction either in somatic cells or in gametes,[6] Here we focus our discussion on the utility of FISH using chromosome painting probes for detecting translocations (Figure 1), which have been found to be stable with time, and therefore can serve as an excellent assay for testing individuals previously exposed to potential genotoxicants.

It should be noted that fluorescent *in situ* hybridization using chromosome painting probes can often yield additional information that is otherwise unobtainable by the traditional chromosome aberration assay alone. In the traditional chromosome aberration assay[7,8] only specific types of structural chromosomal abnormalities are scored. Specific rearrangements of particular chromosomes are not usually identified.

Thus, the ability to detect translocations and other structural chromosomal rearrangements using chromosome painting for monitoring exposure to potential genotoxicants is a powerful approach which is within the reach of the average cytogenetics and genetic toxicology laboratory.

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Point Of View: Who's On First? A Reflection on Euthanasia

Patrick R. Daly, MD

Men may violently disagree about the purposes behind a given act, or about the character of the person who did it, or how he did it, or in what kind of situation he acted; or they may even insist upon totally different words to name the act itself. But be that as it may, any complete statement about motives will offer some kind of answers to these five questions: what was done (act), when or where it was done (scene), who did it (agent), how he did it (agency), and why (purpose).

Kenneth Burke,
"A Grammar of Motives"

1.

"What's the fella's name on first?"
"What's on second, who's on first."

2.

Try this fielding the questions: Who, What, When, Where, Why & How.

'X pulls plug on Y and Y dies' = P
Team A: X = doctor and Y = a terminally ill woman.
Team B: X = hostile son and Y = a terminally ill woman.
Does $P_A = P_B$?

3.

The players take the field.

Question	A	B
Who	doctor	hostile son
What	woman dies	woman dies
When	after consent	before consent
Where	in the open	in the dark
Why	professional judgment	hostile judgment
How	pulls plug	pulls plug

4.

If autonomy were the only issue, we would allow the son to pull the plug so long as his mother consented. Then he would do it in the open and, although his judgment would not be professional, it would not be hostile either. Some might call it beneficent or compassionate and let the matter rest. Who cares if $P_A = P_B$?

Regarding physician assisted suicide, which is based on the same logic as euthanasia, if personal choice were the only issue, proponents would be asking to allow over the counter barbiturates. But we are not talking about s, we are talking about p and a.

5.

The position articulated by Brock[1] and by others[2,3] who are trying to change the law holds that physician assisted suicide and euthanasia are legitimate forms of medical practice. They say that society *should* consent under the right circumstances to allow a doctor to kill a patient.

We are not talking about individual choice; we are talking about a change in the standard of medical practice. We are not being asked to give the son a license to practice medicine; we are being asked to give the doctor a license to kill.

6.

Those who favor euthanasia see a standard already in place that allows doctors to kill: the commonly accepted practice of allowing a patient the right to refuse treatment and allowing the doctor to carry out that patient's wish even when the patient will die. In other words, they answer 'what' the same for the doctor and the hostile son: since the woman dies, they both *kill* the woman.

This is like saying that since rape involves sexual intercourse, then sexual relations between consenting parties is a form of sexual assault.

The relationships of real life have more depth than the relationships of formal logic. Answering the questions 'who' and 'why' and 'where' and 'when' and 'how' bears on answering the question 'what.' We insist that rape differs in kind from intercourse. And Abbott and Costello did not claim to be playing professional baseball.

7.

What difference does consent make?

To pursue the analogy of sexual relations, consent makes all the difference so far as doing violence, but not completely so far as doing right. Even here autonomy has its limits. Does it matter where consenting parties relate sexually, say at Hoxsie Four Corners? Is there a right to commit adultery?

8.

The example of the hostile son does not help to answer the question: what is the doctor doing who pulls the plug? But the question remains: is cooperating with the patient's refusal of care a form of euthanasia?

If Team B recruits a doctor and benches the hostile son, then what happens?

9.

The players take the field.

Question	A	B
Who	doctor	doctor
What	terminal care	euthanasia
When	as long as it takes	when we will not take it
Where	in the open	in the open
Why	common good	autonomous good
How	technology has limits	technology has the last word

10.

We are not talking about the difference between active and passive.[4] An active judgment is made in both cases about what is a reasonable course of treatment.

Opening the door to euthanasia opens the door to the abuse of power.

11.

We may argue about which interventions are reasonable to start, stop or continue when we treat a patient, dying or otherwise. This is not the same as arguing about the reasonableness of introducing a technical intervention designed specifically to kill a patient.

12.

If euthanasia is a legitimate form of medical practice, if B finds precedent in A, this implies that killing equals treating. We are getting close to the paradoxical language of mysticism here, or to the doublespeak of *1984*.

13.

Technology has the last word: if we can't cure you, we can kill you.

14.

Consent, personal choice and 'unilateral authority' are not at issue here.[5,6] Without consent, no treatment is permitted. On this all sides would appear to agree. The question is, if we act openly with consent, what is permitted?

I would answer by way of analogy. Rhode Island state law now holds that it is unprofessional conduct for a physician to engage in sexual relations with a patient, regardless of mutual consent. The same should hold, I would suggest, for any physician who participates in assisted suicide or euthanasia.

15.

There is no significant difference as to active or passive, but there is a difference as to what, when, why and how these actions proceed. Cooperating with a patient's refusal of care differs from and does not establish a precedent for euthanasia.

The question still remains, should euthanasia be permitted?

16.

Let's back up to the remark, killing equals treating. Is this a new, fundamental ethical insight of our time or an open sesame to the abuse of power?

Is this an authentic mystical experience, like Sinai, in that many people are experiencing it close together in time, but unlike Sinai, in that no reference is made to religious authority but only to 'the authority of those whose consciousness has achieved a new stage of development?'[7]

18.

A secular humanism which attempts to establish euthanasia as accepted practice is moving from a skeptical frame of reference to a mythic one. In fact, euthanasia may be the defining rite of the secular myth. Disclaimers to the effect that 'I will examine only secular arguments about euthanasia'[8] do not remove these arguments from the mythic dimension, the dimension of meaning. I would venture to say that the mythic dimension provides the strongest appeal to this whole discussion. I mean, who cares if $P_A = P_B$?

19.

Rather than look to recent developments in biomedical ethics and case law for a precedent for euthanasia, I think that we should look to what used to seem a remote past, the practice of human sacrifice. Acceptance of euthanasia would reinstitute the rite of human sacrifice, to a god we now call 'self-consciousness,' to be performed by priests we now call doctors.

20.

The experiment has already been carried out.

21.

Sanctioning doctors to kill patients will not advance the cause of human freedom, whether or not the ritual is circumscribed by practice guidelines or other tokens of power.

22\.

Doctors should not be given a license to kill.

23\.

Opening the door to euthanasia opens the door to the abuse of power.

24\.

"Then who's playing first?"
"Yes."

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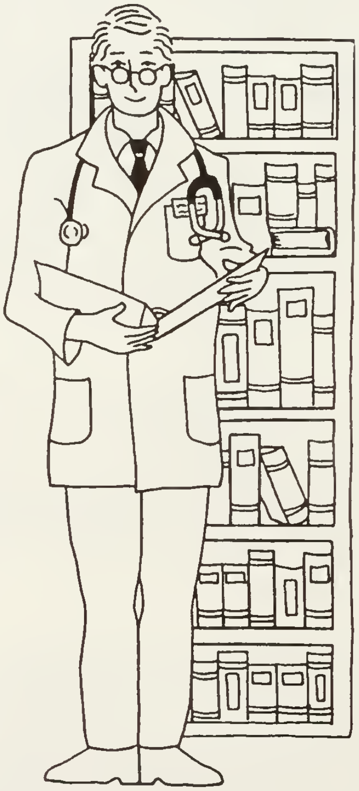

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Health by Numbers

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by William J. Waters, Jr., PhD, and Jay S. Buechner, PhD

Mid-course Review: Healthy Rhode Islanders 2000

Jana E. Hesser, PhD and Jay S. Buechner, PhD

In December 1993 the publication of Healthy Rhode Islanders 2000[1] culminated the efforts of a community-based task force to determine the state's priority health objectives for the decade of the 1990's. The task force, representing a broad spectrum of public health interests in the state, analyzed baseline health data and developed a consensus set of twenty-five health promotion and disease prevention objectives for Rhode Island. They also identified target population groups, major service settings, and proposed implementation strategies for each objective. The twenty-five state health objectives were chosen because they were judged most likely to move Rhode Island toward achievement of the overall goals established for the nation by Healthy People 2000[2].

Guided by this structure, the Rhode Island Department of Health, partner organizations represented on the task force, and collaborating agencies for each objective, have been moving toward achievement of the state's health objectives. In 1995 a mid-course review was undertaken to assess the state's progress towards achievement of these 25 objectives, and to serve as a guidepost for renewing and redoubling our efforts between now and the year 2000.

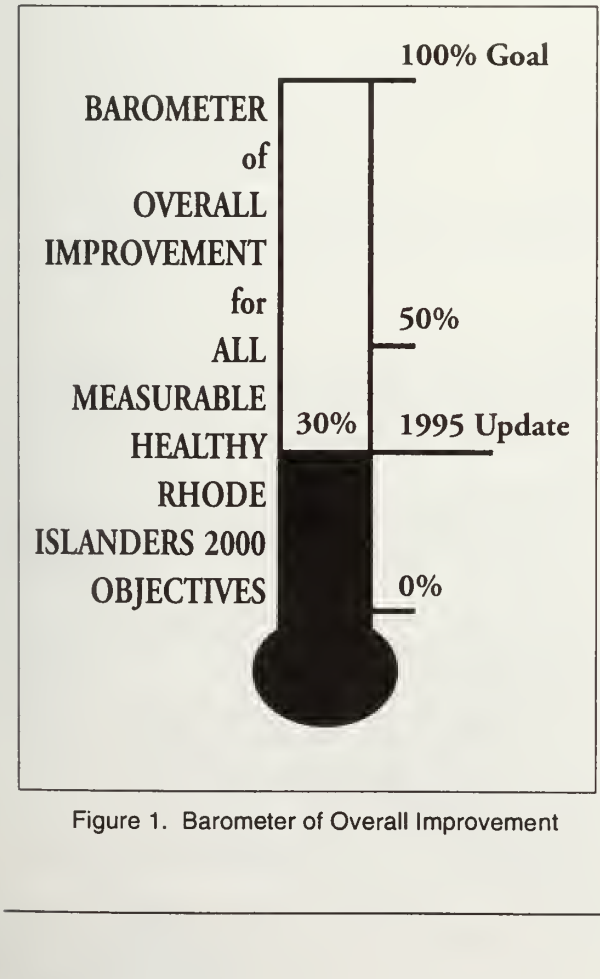

Figure 1. Barometer of Overall Improvement

Released in June 1996[3], results of the mid-course review indicate that much has been accomplished in many areas in a very short time. Based on the twenty Healthy Rhode Islanders 2000 objectives for which data exist to measure change since baseline, there has been a level of overall improvement which is 30% of the way towards goal. (Figure 1)

More specifically, substantial improvement has been made in seven of the twenty measureable Healthy Rhode Islanders 2000 objectives. (Figure 2) Deaths and hospitalizations resulting from injuries of all sorts, whether unintentional, self-inflicted, or resulting from an assault, have decreased substantially. The rate of mortality among newborns and infants is lower than ever recorded previously. Cigarette smoking among adults continues to decrease. The prevalence of high levels of lead in the blood of our children has dropped. The number of persons newly diagnosed with HIV has been held below projections for this period. Drinking water quality has improved.

More modest improvements have been achieved in decreasing Rhode Islanders' exposure to environmental tobacco smoke and in decreasing the number of people who experience illness due to foodborne pathogens. While a substantial proportion of Rhode Island women get screened according to guidelines for breast and cervical cancers, many do not.

In other areas, even more remains to be done. Too many children and adolescents continue to risk their health and years of their lives by smoking cigarettes and using smokeless tobacco. The number of Rhode Islanders who exercise regularly continues to languish, despite the ever-increasing evidence that physical activity reduces the risk of many diseases and promotes mental and physical well-being. Unhealthy dietary habits continue to put much of our population at risk for chronic diseases. The abuse of alcohol and other drugs has increased, with all their physical, social, and economic consequences. Unintended pregnancies show little response to prevention efforts. Immunization rates for the diseases of childhood are inadequate to provide protection for all from outbreaks of these diseases.

Figure 2. Level of Improvement by Objective.

Objective	Substantial Improvement	Some Improvement	No Improvement	Negative Directions	Insufficient Data
1 Physical activity		X			
2 Nutrition				X	
3 Tobacco use		X			
4 Alcohol & drug related problems[1]				X	
5 Unintended pregnancies			X		
6 Suicide & suicide attempts	X				
7 Mental disorders					X
8 Homicides	X				
9 School health education					X[2]
10 Unintentional injuries	X				
11 Work-related injuries		X			
12 Children's blood lead levels	X				
13 Environmental tobacco smoke		X			
14 Radon			X		
15 Drinking water quality	X				
16 Food borne pathogens		X			
17 Oral health		X			
18 Birth outcomes	X				
19 High blood pressure awareness					X
20 Breast & cervical cancer screening		X			
21 HIV prevalence	X				
22 Infectious diseases			X		
23 Immunization		X			
24 Primary care					X[3]
25 Activity limitations					X[3]

[1] Indicators for alcohol and drug use have been added to alcohol and drug related mortality for this measure.
[2] Update data available 1997
[3] Update data available October 1996

The proportion of occupied buildings with unacceptable levels of radon has not changed. Too many Rhode Islanders are lacking adequate dental care. In total, we are in danger of falling short of our targets in thirteen of the twenty measurable objectives.

For five objectives, the extent of improvement cannot be measured because the necessary data are not available, either currently, at baseline, or both. For three of these objectives, those pertaining to school health education, access to primary care, and limitations of activity, the needed data will be available within the next year; for the objectives pertaining to mental disorders and high blood pressure, possible data collection methods are being considered.

Results of the 1995 mid-course review tell us that tremendous strides in achieving a healthier Rhode Island are possible by the Year 2000. Yet doing so will require an expanded partnership among agencies, communities, families, and individuals. Where the level of improvement has been less than acceptable, our efforts need to be reinforced or redirected. Where we have been successful we must consolidate our gains and continue with what has been shown to work. Optimal health is a shared goal. If we build on our current efforts, we can reach these goals and beyond.

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PUBLIC HEALTH BRIEFING

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Judith Feldman, MD, MPH and John P. Fulton, PhD

Update: Clinical Preventive Services

Joann M. Lindenmayer, DVM, MPH and John P. Fulton, PhD

The U.S. Preventive Services Task Force has just released the Second Edition of its *Guide to Clinical Preventive Services*, the essential reference on the effectiveness of clinical preventive services first released in 1989. The second edition is much expanded, indicative of the growth in knowledge over the past decade. Like its predecessor, the 1996 *Guide* carefully assesses the published literature on the effectiveness of a broad range of clinical preventive services, clarifies issues regarding their use, and makes clear recommendations for the clinician.

Over the next few months, we intend to focus on some of the hottest issues in the 1996 *Guide*, including those relevant to the following clinical preventive services:

Aspirin prohphylaxis for the primary prevention of myocardial infarction
Counseling to promote physical activity
Screening for high blood cholesterol and other lipid abnormalities
Screening for breast cancer
Screening for cervical cancer
Screening for colorectal cancer
Screening for family violence
Screening for ovarian cancer
Screening for oral cancer
Screening for postmenopausal osteoporosis
Screening for prostate cancer

Meanwhile, we have listed Task Force recommendations for these services in the adjoining table. Some, like counseling to promote physical activity, should come as no surprise to anyone. Others, like the clear recommendation *against* prostate cancer screening, are hotly contested in the literature. Either way, we hope our treatment of these issues over the next few months will prove interesting and useful to the clinician.

As a health department, we recognize the essential contribution of clinicians to the prevention of disease and disability in our community. It is our goal to help clinicians in this endeavor by supporting a practice environment in which clinical preventive services of proven impact may be applied to maximum effect in the Rhode Island population.

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Selected Recommendations of the U.S. Preventive Services Task Force

Aspirin prophylaxis for the primary prevention of myocardial infarction:

There is insufficient evidence to recommend for or against routine aspirin prophylaxis for the primary prevention of myocardial infarction (MI) in asymptomatic persons. Although aspirin reduces the risk of MI in men aged 40-84, its use is associated with important adverse effects, and the balance of benefits and harms is uncertain. If aspirin prophylaxis is considered, clinicians and patients should discuss benefits and risk for the individual before beginning its use.

Counseling to promote physical activity:

Counseling patients to incorporate regular physical activity into their daily routines is recommended to prevent coronary heart disease, hypertension, obesity, and diabetes. This recommendation is based on the proven benefits of regular physical activity; the effectiveness of clinician counseling to promote physical activity is not established.

Screening for high blood cholesterol and other lipid abnormalities:

Periodic screening for high blood cholesterol is recommended for all men ages 35-65 and women ages 45-65. There is insufficient evidence to recommend for or against routine screening of asymptomatic persons over age 65, but recommendations to screen healthy men and women ages 65-75 may be made on other grounds. There is also insufficient evidence to recommend for or against routine screening in children, adolescents, or young adults. Recommendations for screening adolescents and young adults with risk factors for coronary disease, and against routine screening in children, may be made on other grounds. There is insufficient evidence to recommend for or against routine screening for other lipid abnormalities. All patients should receive periodic screening and counseling regarding other measures to reduce their risk of coronary disease.

Screening for breast cancer:

Routine screening for breast cancer every 1-2 years, with mammography alone and annual clinical breast examination (CBE), is recommended for women aged 50-69. There is insufficient evidence to recommend for or against routine mammography or CBE for women aged 40-49 or aged 70 and older, although recommendations for high-risk women aged 40-49 and healthy women aged 70+ may be made on other grounds. There is insufficient evidence to recommend for or against the use of screening CBE alone or the teaching of breast self-examination.

Screening for cervical cancer:

Routine screening for cervical cancer with Papanicolaou (Pap) testing is recommended for all women who are or have been sexually active and who have a cervix. Pap smears should begin with the onset of sexual activity and should be repeated at least every 3 years. There is insufficient evidence to recommend for or against an upper age limit for Pap testing, but recommendations can be made on other grounds to discontinue regular testing after age 65 in women who have had regular previous screenings in which the smears have been consistently normal. There is insufficient evidence to recommend for or against routine screening with cervicography or colposcopy, or for screening for human papilloma virus infection, although recommendations against such screening can be made on other grounds.

Screening for colorectal cancer:

Screening for colorectal cancer is recommended for all persons aged 50 and older with annual fecal occult blood testing (FOBT), or sigmoidoscopy (periodicity unspecified), or both. There is insufficient evidence to determine which of these screening methods is preferable or whether the combination of FOBT and sigmoidoscopy produces greater benefits than does either test alone. There is also insufficient evidence to recommend for or against routine screening with digital rectal examination, barium enema, or colonoscopy, although recommendations against such screening in average-risk persons may be made on other grounds. Persons with a family history of hereditary syndromes associated with a high risk of colon cancer should be referred for diagnosis and management.

Screening for family violence:

There is insufficient evidence to recommend for or against the use of specific screening instruments to detect family violence, but recommendations to include questions about physical abuse when taking a history from adult patients may be made on other grounds. Clinicians should be alert to the various presentations of child abuse, spouse and partner abuse, and elder abuse.

Screening for ovarian cancer:

Routine screening for ovarian cancer by ultrasound, the measurement of serum tumor markers, or pelvic examination is not recommended. There is insufficient evidence to recommend for or against the screening of asymptomatic women at increased risk of developing ovarian cancer.

Screening for oral cancer:

There is insufficient evidence to recommend for or against routine screening of asymptomatic persons for oral cancer by primary care clinicians. All patients should be counseled to discontinue the use of all forms of tobacco and to limit consumption of alcohol. Clinicians should remain alert to signs and symptoms of oral cancer and premalignancy in persons who use tobacco or alcohol.

Screening for postmenopausal osteoporosis:

There is insufficient evidence to recommend for or against routine screening for osteoporosis with bone densitometry in postmenopausal women. Recommendations against routine screening may be made on other grounds. All postmenopausal women should be counseled about hormone prophylaxis and be advised of the importance of smoking cessation, regular exercise, and adequate calcium intake. For those high-risk women who would consider estrogen only to prevent osteoporosis, screening may be appropriate to assist treatment decisions.

Screening for prostate cancer:

Routine screening for prostate cancer with digital rectal examinations, serum tumor markers (e.g., prostate-specific antigen), or transrectal ultrasound is not recommended.

Source: *Guide to Clinical Preventive Services, 2nd ed.*

Vital Statistics

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health
Edited by Roberta A. Chevoya

Rhode Island Monthly Vital Statistics Report
Provisional Occurrence Data from the Division of Vital Records

Vital Events

	Reporting Period		
	March 1996	12 Months Ending with March 1996	
	Number	Number	Rates
Live Births	1,092	13,931	14.0*
Deaths	820	9,628	9.7*
Infant Deaths	(3)	(93)	6.7#
Neonatal deaths	(1)	(71)	5.1#
Marriages	388	7,579	7.6*
Divorces	320	3,544	3.6*
Induced Terminations	559	5,557	398.9#
Spontaneous Fetal Deaths	75	1,150	82.5#
Under 20 weeks gestation	(73)	(1,093)	78.5#
20+ weeks gestation	(2)	(57)	4.1#

* Rates per 1,000 estimated population
# Rates per 1,000 live births

Underlying Cause of Death

	Reporting Period			
	Sept. 1995	12 Months Ending with Sept. 1995		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	276	3,350	336.2	4,466.0
Malignant Neoplasms	189	2,450	245.9	6,954.0
Cerebrovascular Diseases	38	618	62.0	535.0
Injuries (Accident/Suicide/Homicide)	28	322	32.3	6,031.5
COPD	26	400	40.1	335.0

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.
(b) Rates per 100,00 current estimated population of 996,325
(c) Years of Potential Life Lost (YPLL)

Note: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

Philately in Medicine

John Tierney

The Human Circulatory System on Stamps

The great English physician and experimental physiologist, William Harvey (1578 - 1657) was the acknowledged father of cardiac and circulatory physiology [Argentina, 1959, figure 1] and was the first to accurately describe the circulatory flow of blood unidirectionally from the heart, through the arteries, and then within the veins conveying the blood back to the heart in a cyclic manner [Hungary, 1973, figure 2].

In 1628, Harvey published a 72 page text entitled *"Exercitatio de Motu Cordis et Sanguinis in Animalbus"* (Experiments on the Cardiac Movement of Animals) which firmly established a rational foundation for modern cardiac physiology. Sherwin B. Nuland, MD, in his book *"Doctors: The Biography of Medicine"* stated: "For it was he [Harvey] who bestowed the greatest gift by one man to the science and art of medicine - the discovery of the circulation of blood." Nuland further notes: "With the unique exception of Louis Pasteur, he [William Harvey] is the most honored of all great contributors of medical knowledge."

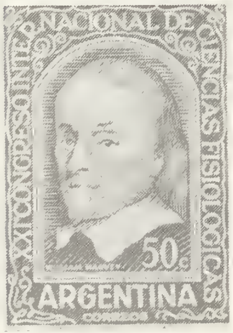
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Figure 1

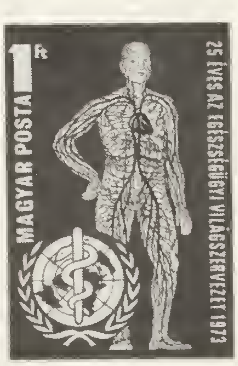
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Figure 2

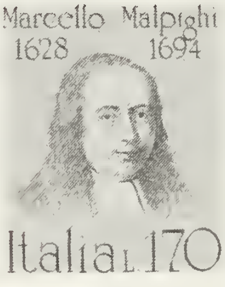
Marcello Malpighi
1628 1694
Italia L.170

Figure 3

Harvey's original text, *de Motu Cordis,* has also emerged in recent years as the most monetarily valuable medical book ever written. Each of the few remaining copies of the first edition were priced at $300,000 in 1988.

The concept of an enclosed capillary network uniting the arterial and venous components of the circulatory system was proposed by Marcello Malpighi (1628 - 1694) the great Italian experimental physiologist [Italy, 1978, figure 3] a graduate of Bologna's great medical school in 1653. He then accepted a prestigious professorship at Pisa University. Because many members of the Pisa medical faculty still supported the teachings of Galen (130 - 201 ?) [Yemen, 1977, figure 4] Malpighi, and his physiologic concepts, became victims of "brutal and cruel persecution" and he was finally forced to depart from Pisa in 1669. He returned to his alma mater, Bologna, where he stayed for the remainder of his professional career, except for a short teaching interval at the University of Messina in Sicily.

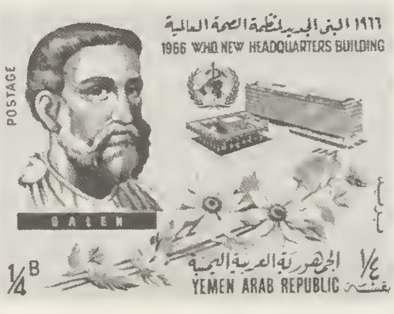
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Figure 4

Malpighi headed a division of structural anatomy at Bologna, making notable contributions both to the fields of structural and physiological medicine. On the 900th anniversary of the founding of the school at Bologna, a stamp was issued to honor this memorable occasion [Italy, 1988, figure 5].

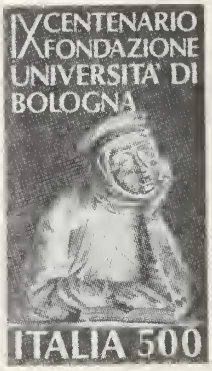
IX CENTENARIO FONDAZIONE UNIVERSITA' DI BOLOGNA
ITALIA 500

Figure 5

CORRESPONDENCE:
J. Tierney

THE RHODE ISLAND MEDICAL JOURNAL

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Issued Monthly under the direction of the Publications Committee

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PROVIDENCE, R.I., JANUARY, 1917
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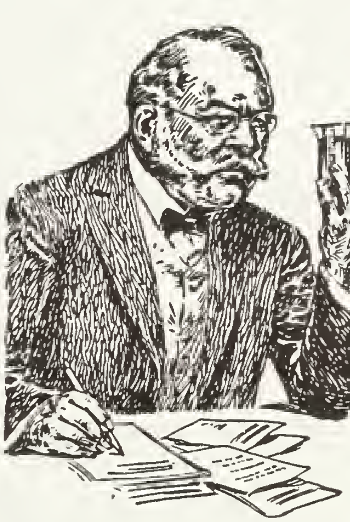
NINETY YEARS AGO

[SEPTEMBER, 1906]

This issue of the *Journal* is devoted to a series of papers analyzing clinical neurasthenia. The first, entitled The Etiology and Symptomatology of Neurasthenia with Special Reference to the Mental Disorder Psychasthenia is written by William McDonald, MD of Providence. He notes that normal fatigue involves both the extra and the intracerebral nervous system and that the symptoms of exhaustion show an inextricable admixture of disturbances of both. According to the variety of activity producing the fatigue, however, disturbance of either the higher cerebral or extracerebral functions may predominate. For example, after a night of excessive mental labor an individual commonly experiences feelings of nervousness, weariness, irritability, depression, loss of ambition, and incapacity for further work. The symptoms of this ensuing psychasthenia may then be separated into two categories: disturbance of function of intellectual activities; and secondly, "feelings of incompletude." Symptoms may embrace such phenomena as a variety of phobias, instability, indecision, ennui and shame. He concludes: "Every psychasthenic tends toward the fixation and systemization of his morbid mental processes, so that even after his mental tension has been raised and the exhaustion relieved, a permanent vicious habit of thought, of act, and of feeling may remain as a relic. The early stage, before habit has been formed, is the time for treatment."

John E. Donley, MD writes on the psycho-physical mechanisms of neurasthenia. He believes that neurasthenia may provide a series of phenomena "which are still consonant with health, but which under certain conditions, pass over into disease, or in other words, neurasthenia." The author concludes by summarizing the thoughts of a typical neurasthenic patient: "I feel tired and weary; I experience a sense of lassitude and general discomfort; my head aches; my appetite is poor; my memory untrustworthy; my mind has lost its grasp on reality, and I find difficulty in concentrating long upon what I am doing. Little things trouble me, and I feel as though I can scarcely keep myself together, while I have not the energy to do things as well as when I am not fagged out."



A further paper on neurasthenia, its diagnosis and prognosis is offered by Henry C. Hall, MD. Much of his presentation is devoted to a careful listing of distinctions between neurasthenia and hysteria. The former produces symptoms which are largely subjective against a background of a uniformly depressed state of consciousness; while the latter displays objective symptoms, with an irregular clinical course and only occasionally associated with depression. Fatigue is appreciably more common in the former. Paresthesia may be encountered in neurasthenia while hypesthesia, hyperesthesia and even anesthesia may be seen in hysteria. The author notes: "He who has lost the desire to live and as ardently longs for death shows a departure from the normal consistent only with insanity. He who is a self-accuser as to sexual practices may recover. Not so the wretch whose sense of decency is paralyzed."

FIFTY YEARS AGO

[SEPTEMBER, 1946]

The lead article, written by John P. Hubbard, MD and colleagues, describes their seven years of experience in the convalescent care of children with rheumatic fever at the Sharon Sanatorium. A total of 201 chiuldren were part of this study, the majority admitted during the active phase of their rheumatic infection. About half showed evidence of heart disease. Any satisfactory plan of management for convalescent care of rhuematic children, state the authors, must take into consideration two factors: [1] suitable medical care and [2] attention to the development of the child's whole personality during the period of his convalescence. They conclude: "It is fair to state that the results of this experience demonstrate that an open air sanatorium may be not only satisfactory but advantageous. "

Francesco Ronchese, MD discusses the management of cutaneous hemangiomas. "The question of treating or not treating infantile hemangiomas, in view of the fact that the majority of them disappear spontaneously, is reviewed and discussed. Because not all hemangiomas disappear and because with proper treatment the risk involved is very small and the sequelae inconsequential, it is advisable to treat the majority of them, leaving untreated only those which, for size and location, are suitable for later surgical removal, should they not disappear."

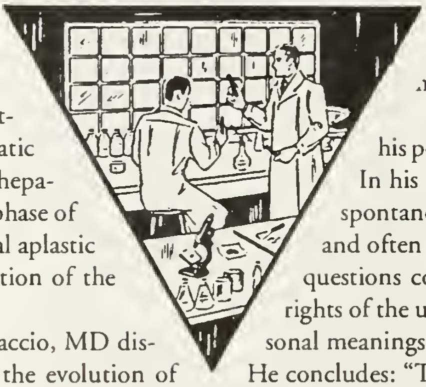
Jack Savran, MD outlines his successful use of diethylstilbesterol in the prevention or mitigation of orchitis following acute mumps infection in army personnel.

Lewis Abramson, MD and Frank Masyner, MD describe the clinical course and autopsy findings of a 12 year old female who developed Waterhouse Friderichsen syndrome.

An article from the Hospital Association of Rhode Island describes the history and many community contributions of the Woonsocket Hospital since its beginning on October 10, 1888.

Twenty Five Years Ago

[September, 1971]



Maurice Albala, MD, Sze K. Kaan, MD and Charles A. Pan MD describe the case of a 21 year old white male who was admitted to the hospital because of asymptomatic jaundice. A diagnosis of progressive viral hepatitis was made. During the convalescent phase of the hepatitis, the patient developed a fatal aplastic anemia presumed to be a rare complication of the hepatitis.

A.V.Migliaccio, MD and A.J. Migliaccio, MD discuss the role of radical splenectomy in the evolution of Hodgkin's disease. The authors believe that the procedure is safe and permits some measure of accurate staging of the disease.

M. Kakvan, MD and colleagues evaluate the extent of collateral myocardial blood flow in experimental animals following long term implantation of the internal mammary artery. Their experimental results support the view that "... the Vineburg procedure provides functional revascularization of the myocaridum."

Anthony P. Chatowsky, MD provides his personal thoughts on therapeutic abortion. In his view, "abortion of any type, natural and spontaneous or artificially induced, is a complex and often emotionally charged subject. It involves questions concerning the rights of the mother, the rights of the unborn, the rights of society, and the personal meanings and consequences to those concerned." He concludes: "The psychiatrist is directly involved with the abortion question. He is in a unique position to evaluate the conscious and unconscious motivations involved, to look at the personal and social factors, and to consider the future for both mother and child."

A brief biography of Isaac Kaminer, MD [1834-1901] who was physician, poet and satirist, is provided by Harry Savitz, MD.

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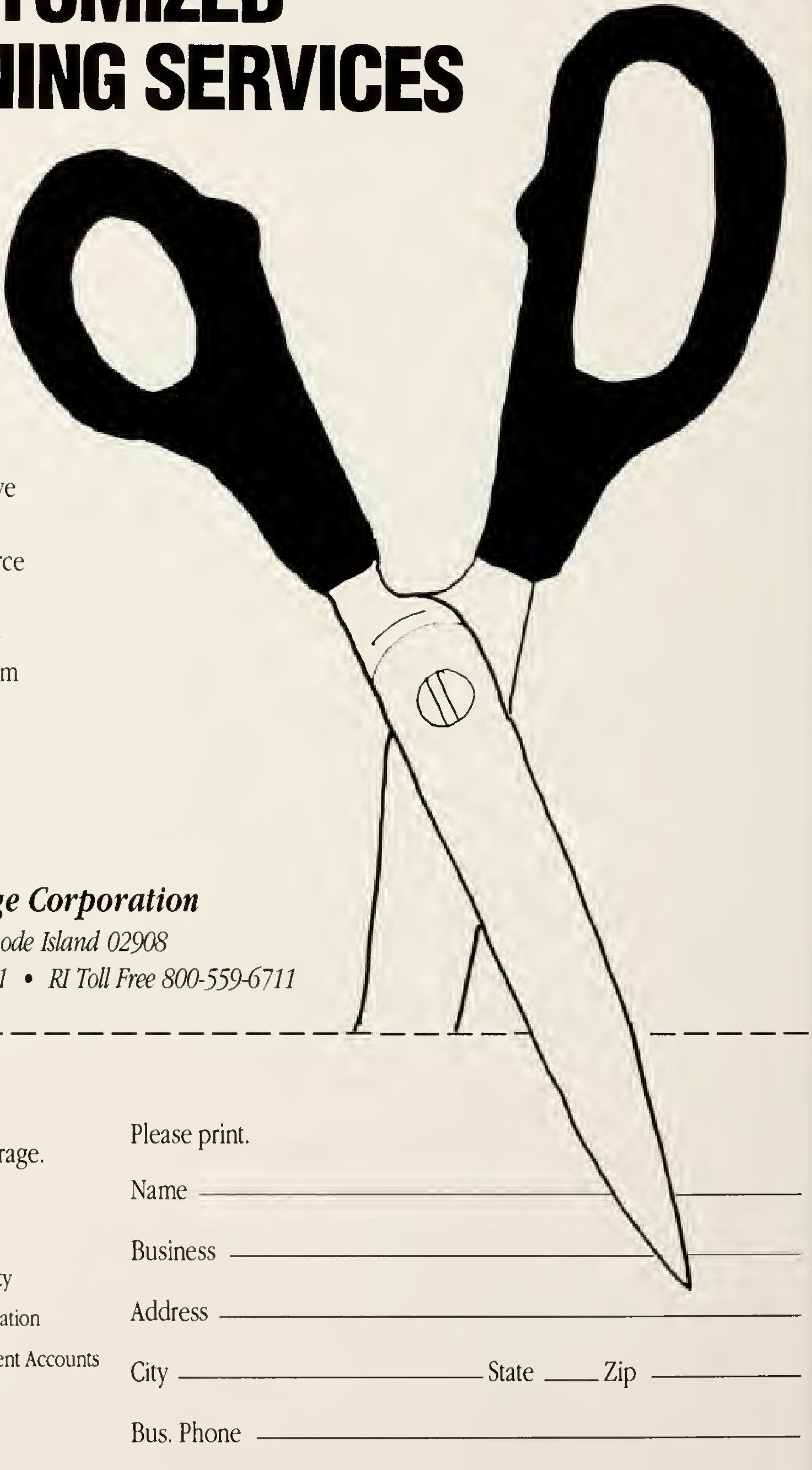

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Cover: Anne of Austria visiting the great hospital ward of Charité c. 1640
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COMMENTARIES

A Profile of the Rhode Island Chapter of the American College of Physicians

The Rhode Island chapter of the American College of Physicians (ACP) is the local unit of the largest medical specialty society in the United States. Nationally, ACP has 89,000 members trained in internal medicine and related subspecialties. ACP was founded in 1915 to enhance the quality and effectiveness of health care by fostering excellence and professionalism in the practice of medicine. ACP publishes *Annals of Internal Medicine*, the most widely-cited medical specialty journal in the world.

ACP has long been a leader in medical education for internists, sponsoring hundreds of graduate medical education courses across the U. S. The College is a leader in medical informatics, publishes books for practicing physicians, and was perhaps the first physician organization to develop clinical practice guidelines for diagnostic testing and screening. To date, it has published more than 160 evidence-based guidelines. Active in health and public policy, it has issued position papers on such topical concerns as inner city health care, insurance reform, voluntary insurance purchasing pools and universal health coverage. The College's Washington office works on regulatory and legislative issues affecting physicians.

ACP works with other medical organizations, such as the AMA, on both the local and national level. It sponsors two organizations: the Council of Specialty Societies, with representatives from all the internal medicine subspecialties, and the Council of Medical Societies, with representatives from 20 medical and public health groups related to internal medicine, including the American Geriatrics Society, American Public Health Association, and Society for Adolescent Medicine.

Abbreviations Used

ACP	American College of Physicians
AMA	American Medical Association
CME	Continuing Medical Education
HMO	Health Maintenance Organization

The ACP Rhode Island chapter has been active since 1927, with Frederic J. Farnell, MD, of Providence, serving as its first governor. The chapter was incorporated in June 1979, and is governed by an executive council and various committees. ACP governors are elected to four-year terms by chapter members. They manage chapter activities and represent members both at the national level and on the College's board of governors, an advisory group to the College's policy-making body, the ACP Board of Regents.

Michele Cyr, MD, is the current Rhode Island chapter governor. Preceding Dr. Cyr as ACP governor for Rhode Island were Joseph A. Chazan, MD, who served from 1990 to 1994 and H. Denman Scott, MD, who served from 1986 to 1990. Other ACP Rhode Island Governors following Dr. Farnell were Alex Burgess, MD, Herman Lawson, MD, Marshall Fulton, MD, Irving Beck, MD, William Fischer, Jr., MD, Milton Hamolsky, MD, Joseph DiMase, MD, and Edward Iannuccilli, MD.

Locally, the chapter holds two annual meetings for members to update their clinical knowledge, and awards CME credit. The annual spring scientific meeting includes an ACP Associates program for residents and fellows from Brown University-affiliated teaching hospitals. The Associates program has grown dramatically over the years, with 13 oral abstracts and 100 posters presented at the 1996 meeting. This issue of *Medicine and Health/Rhode Island* contains the abstracts or papers presented during the March, 1996, ACP meeting in Warwick, R.I. The RI ACP sponsors the annual internal medicine update, which will be held this year at the Newport Doubletreee Hotel on Goat Island, Newport, on October 29, 1996. Non-ACP members and medical students are welcome to attend. Please call (401) 444-8537.

With 501 members, the ACP Rhode Island chapter is considered a small-to-medium sized ACP chapter. Three Rhode Island members are ACP masters and 114 are fellows. ACP masters are highly distinguished physicians who have achieved recognition in medicine for preeminence in practice or medical research. The three Rhode Island ACP masters are Paul Calabresi, MD, Charles Carpenter, MD, and Milton Hamolsky, MD. ACP fellowship is an honor achieved by recognized personal integrity, superior competence in internal medicine, professional accomplishment and demonstrated scholarship. Overall, membership in the Rhode Island chapter has grown by 16.5% over the last five years.

ACP members in Rhode Island work in a variety of settings: 20.4% are self-employed in solo practice, 22.4% are in a group practice, 24.4% are employed by non-government hospitals, 5.2% are in a two-physician practice, 3.7% are affiliated with the federal government and 3.0% are in a staff-model HMO. The Rhode Island practice profile is similar to ACP's nationally: 66.1% practice general internal medicine (compared with 64.3% nationally), 8.1% treat cardiovascular disease (compared with 6.2% nationally), with fewer practicing in the various other subspecialties of internal medicine. These figures were supplied by ACP chapter (and national) members who could list more than one category of employment and internal medicine subspecialty.

ACP chapters bring local concerns to the national level at twice-yearly Board of Governors meetings through resolutions, through commentary on College policy papers under development, through participation on national committees, and through participation in an active College-sponsored E-mail forum.

Rhode Island ACP members visited their state legislators in Washington last year during ACP's Legislative Action Day. Many attended the ACP national meeting, which last year was held in San Francisco and attracted more than 6,000 members nationwide.

Each year the RI chapter bestows the Irving A. Beck Award to an outstanding internist in the state. The award is named for Irving Beck, a native Rhode Islander and Brown graduate who has had a long and distinguished career in medicine. He is a fellow of the ACP and was governor of the Rhode Island chapter from 1962 to 1968. The 1996 Beck award recipient was Herbert Rakatansky, MD, internist and gastroenterologist. Dr. Rakatansky is president of the Miriam Hospital medical staff, and is active in the Providence Medical Association and the Rhode Island Medical Society. Former recipients of the Beck award include Richard K. Mead, MD, Henry Izeman, MD, Costas Georas, MD, Hugh Holdsworth, MD, Janis Gailitis, MD, Robert Lewis, MD, and Michael DiMaio, MD.

– Michele G. Cyr, MD

Michele G. Cyr, MD, is Director, Division of General Internal Medicine, Rhode Island Hospital, and the governor, American College of Physicians, Rhode Island Chapter.

An Old Diagnostic Test for Plague

To those unschooled in celestial mechanics, a comet must surely seem to be a terrifying intruder wandering across the orderly array of the stars, much like a hyperactive adolescent rampaging across the altar during solemn church services: unannounced, unapologetic and unpredictable.

To primitive humans constantly beset by catastrophe, any natural event outside the normal cycle of things - such as a comet - must necessarily have caused much anxiety. It could only happen, they might have conjectured, because some evil act had been committed and a higher authority had responded with an expressly directed sign heralding some imminent peril. It seems to be a common human trait to blame great enigmas or disasters on personal transgressions, a curious kind of egocentricity. And were a comet to be dispatched for each human transgression, some realistic observers had speculated, the night skies would be ablaze with light and streetlights would then be unneeded.

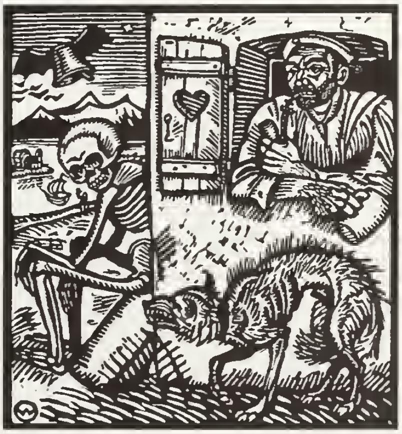
During the great northeast regional electrical blackout of the late 1960's, newspapers reported the story of an agitated Bronx youth, full of remorse, who turned himself into the police claiming that the immense blackout was his personal fault. Earlier that evening, in anger, he had struck a streetlight with his baseball bat; and within seconds all the streets were darkened.

Aristotle, convinced that the firmament was changeless, taught that comets must therefore represent an earthly exhalation condensing in the sublunar atmosphere to create fiery pathways. The imperial Chinese court was obsessed with comets as forecasters of earthly events, and for over a millennium maintained astronomers who scanned the skies for aberrant objects such as comets. These events were then carefully recorded and linked with unique happenings such as the deaths of emperors.

Comets are rarely reported in the Scriptures except in Revelation where there is mention of "a great star fell from heaven, blazing like a torch," amidst much apocalyptic ferment including plagues.

Some ancient observers were satisfied merely to record the dates and celestial movements of each new comet. Others, convinced that they were divinely dispatched omens, sought instead to determine with what earthbound tragedy they coincided. The comet of 371 BC, for example, was visible just before the great coastal earthquakes of Greece. Josephus writes that a comet hung transfixed over Jerusalem the year before the city was destroyed by Emperor Vespasian. On the other hand, the death of Julius Caesar went unannounced in the skies: no comets foretold his assassination. Later Roman historians rectified this by explaining that the Caesarian comet must surely have been obscured by clouds. Shakespeare agreed and had Caesar's anxious wife exclaim: "When beggars die there are no comets seen. The heavens themselves blaze forth the death of princes."

Monastic chroniclers set to parchment much of recorded history during the Middle Ages: events within their abbeys, miracles in the secular world, the succession of kings, the



droughts, the floods, the many plagues and particularly the lunar eclipses and cometary transits. The shape, color and zodiac relationships of each comet was carefully documented with great attention devoted to variations in the hairy tail of each comet. [The word, comet, is derived from a Greek word meaning hair.] Many of these commentaries demonstrated an incontestible relationship between comets and earthly disaster, particularly pestilence. Later historians saw only an "amiable credulity" in these correlations since hardly any year during that era had been free of plague, famine, war or the death of some great leader. Albertus Magnus, the leading scholar of his day wrote that "comets may signify wars and the death of kings." The Bayeux Tapestry which depicted the events surrounding the 1066 Norman invasion of England displays a prominent comet which had appeared months before the invasion and thus presumably presaging King Harold's death on the battlefield. The comet of 1347 was widely interpreted as predicting the onset of the Bubonic Plague later that year.

Through much of the 16th century, faith remained stronger than skepticism. Medical students devoted more time to astrology than anatomy and comets continued to represent either the condensed sublunar fumes of human sin ["the thick smoke of human sin, rising every minute"] or portentious fireballs propelled by an angry diety. Luther proclaimed: "The heathen writes that the Comet may arise from natural causes; but God creates not one that does not foretoken a sure calamity."

The comet of 1577, however, marked the hesitant transition toward a qualified acceptance of comets as natural phenomena moving in accordance with the laws of nature. This 1577 comet permitted Tycho and others to demonstrate by parallax studies that it existed in space well beyond the moon. Cautious suggestions were offered that comets might even have predictable orbits, much like the known planets. Nonetheless the Bubonic Plague of London, in 1665, was unwaveringly attributed to the great comet of the prior year. Said one influential text: "And as the inevitable effect of comets, we must expect sickness, diseases, mortality and more especially the sudden death of Great Ones." Even educated John Milton intoned: "The comet from its horrid hair shakes pestilence and war."

Edmund Halley mapped the trajectory of the 1682 comet, concluding that it followed an eccentrically elliptical course around the sun and, furthermore, that it was the same as the comets of 1455, 1531 and1607. He confidently predicted that it would return again late in the year 1758 following a 76 year cycle. On Christmas eve of 1758, the apparition did indeed return in the very sector of the sky foreseen by Halley [who died some 16 years before his prediction had been fulfilled.] . Skepticism and even humor were now replacing uncritical awe. Swift, for example, reflected that old men and comets have been reverenced for the same reason: their long beards and pretenses to foretell events. And Sam Johnson rhymed: "If at your coming princes disappear, Comets come every day and stay a year."

By the late 20th century, the influence of astrology - except in the minds of a rare White House occupant - had now retreated substantially. Here and there, perhaps, were some quivering souls who persisted in hearing messages from on high and still viewed comets as messengers of imminent pestilence. But for most people, splendid comets were revealed to be mere fragments of cosmic debris jaywalking across prescribed planetary orbits - and their predictive abilities were reduced to transcendental hogwash.

Twenty centuries ago, with uncommon insight, there was the voice of Seneca: "There are many things whose existence we allow, but whose character we are still in ignorance of. Why should we be surprised, then, that comets, so rare a sight in the universe, are not embraced under definite laws, or that their beginning and end are not known seeing that their return is at long intervals ? The day will yet come when the progress of research will reveal the mysteries of nature that are now concealed. The day will come when posterity will be amazed that we remained ignorant of things that will to them seem so plain. Let us be satisfied with what we have discovered, and leave a little truth for our descendants to find out."

– Stanley M. Aronson, MD

The Man Who Understood Mosquitoes

In some parts of the world, particularly regions oppressed by malaria, August 20 is celebrated as Mosquito Day. It is a perplexing holiday since most people do not happily honor their oppressors. At first glance, the ritual might be akin in bizarreness to a society which venerates the drunk-driver or the plague-carrying flea. In truth, though, the Day pays homage not to the mosquito but to the man who indicted it as the vector responsible for malaria.

On August 20, 1897, a Scottish physician named Ronald Ross, then an officer in the Indian Medical Corps, completed his painstaking studies of the female anopheline mosquito, demonstrating conclusively the presence of the malarial parasite within its stomach and salivary glands. His meticulous inquiries, aided only by an ancient monocular microscope with cracked lenses, provided the first clear understanding of how the parasite of malaria travelled from person to person by the blood-seeking impulses of the female mosquito.

In the days of the British Raj, malaria killed about one million persons each year. This remorseless toll befell India year upon year and was stoically accepted by both ruler and ruled with the same fatalism as the annual monsoon. Quinine was an effective, although expensive, medication for the suppression of malaria. But the entire national yield of the drug could not provide prophylaxis for more than about 6% of the vulnerable Indian population. Until the production of quinine could be substantially increased, a curative program for the control of malaria was therefore unattainable.

The studies undertaken by Ross did more than specify the carrier and pathogenic cycle of malaria; they yielded a threefold strategy by which the disease might be prevented: deprive the mosquito of its breeding grounds; kill the adult mosquito; and create physical barriers, such as screening, whereby anopheline contact with humans was diminished. Ross had exhaustively investigated the lifestyle of the anopheline species, its flying range, its nutritional needs, its biological and breeding characteristics, its vulnerabilities. His recommendations, when scrupulously followed [as in the Malaysian peninsula], resulted in dramatic reductions in malarial incidence. Within a few years, his protocols also provided the design for similar studies in Cuba by Walter Reed and colleagues on another mosquito-borne disease, yellow fever, again resulting in a striking disease suppression. The Ross regimen was also adopted by the engineers building the Panama Canal prompting the Surgeon General, W.G. Gorgas, to state: "It seems to me not extreme, therefore, to say that it was your discovery of this fact that enabled us to build the Canal at the Isthmus of Panama." In 1902 Sir Ronald Ross was awarded the Nobel Prize in Medicine.

Ross was born just south of the Himalayas in 1857, during the twentieth year of Victoria's interminable reign. His father, a descendant of an illustrious Scottish family of military leaders, was the commanding general of British forces in eastern India. Ross first encountered England when he was shipped back for entrance into a boarding school. His first, and indeed enduring, inclination was to become a writer, perhaps even a musician. Family insistence, however, compelled him to register as a most reluctant student in St. Bartholomew's Medical School, London. Upon graduation, he complied with his father's wishes and enlisted in the Indian Medical Service for a decade of duty in eastern India.

In 1894 Ross returned to London for further graduate training in the emerging science of bacteriology. Upon returning to India he now dedicated his energies, beyond his customary medical duties, to a search for the pathway by which malaria was transmitted. Following Manson's seminal discovery that a mosquito was responsible for the spread of a parasitic disease called filariasis, Ross focused his attention on this insect as a possible malarial vector. And after three years of intensive search, Ross was finally able to demonstrate which mosquito genus was the carrier as well as clarify the specific dynamics of the infective pathway. In the course of these inquiries, Ross employed his extensive knowledge of mathematics to develop a series of fundamental equations demonstrating the interrelationship of such variables as mosquito density, rates of active malarial cases, rain fall, ambient tempera-

ture variation and numbers of bites per person per day. The Ross equations have since been effective in unravelling the epidemiologic complexities of yet other parasitic disorders and have served to immortalize the name of Sir Ronald Ross in the annals of a branch of applied mathematics called pathometrics.

During all of these parasitological, medical and mathematical undertakings, Ross maintained an unwavering interest in creative writing. A steady stream of successful novels, plays and books of poetry attest to his writing skills. Many literary critics, perhaps not conversant with the malign nature of malaria, regretted that Ross devoted *any* time to his medical studies. They regarded his extensive body of writings as sufficient justification for the Nobel prize, but in literature rather than medicine.

A physician as sensitive as Ross could not but be aggrieved by the evil enormity of malaria, murdering some million Indians each year. It preoccupied his thinking from the moment of his arrival in India, influencing both his scientific pursuits and even the content of his poetry. In 1895, upon his return to India, he composed a brief poem distilling in a few poignant sentences the wrenching sense of inadequacy experienced by any physician who must tell his patient that no cure is yet available for his ailment but that medicine unceasingly seeks the laws, the rules by which diseases are secretly conveyed from one unsuspecting person to another.

* * *

In this, O Nature, yield I pray to me.
I pace and pace, and think and think, and take
The fever'd hands, and note down all I see,
That some distant light may haply break.

The painful faces ask, can we not cure?
We answer, No, not yet; we seek the laws.
O God, reveal thro' all this thing obscure
The unseen, small, but million-murdering cause.

– **Stanley M. Aronson, MD**

Research Abstracts Presented by Resident Physicians During Spring 1996 Meeting of the American College of Physicians

Fred J. Schiffman, MD

The Tenth Annual Meeting of the Rhode Island Chapter of the American College of Physicians (ACP) and the Department of Medicine at Brown University was held at the Radisson Airport Hotel on March 26 and 27, 1996. Participation by Brown University medical residents broke previous records, with 77 poster presentations and 13 oral presentations.

In the presence of a large number of senior physicians, medical residents presented their posters on Tuesday evening, March 26th from 6- 8:00 p.m.

Dr. Rowen K. Zetterman, MD, FACP, the official College representative, viewed posters and interacted with presenters during the evening. Each Brown-affiliated hospital was represented by poster presentations.

As usual, poster displays remained standing for the duration of the meeting so that participants could view the posters and continue to discuss the work with the authors.

Topics of poster and oral presentations were diverse and provocative, including unusual presentations of tuberculosis, a review of the adenovirus epidemic which struck Rhode Island, myopericarditis associated with *Campylobacter jejuni*, L-Dopa induced respiratory dysfunction, and the 19th century treatment of tachycardia with bugle weed.

On Wednesday morning, March 28, 1996, Dr. Michele Cyr, ACP Governor, Rhode Island Chapter, opened the meeting and welcomed Dr. Zetterman, who gave a "College Update." Several oral presentations were given, followed by mini-symposia for the internist, which included updates on dermatology by Dr. Charles MacDonald, ophthalmology by Dr. William Tsiaris, and orthopedics by Dr. Paul Fadale.

The Irving Beck Award, presented annually at this meeting to an outstanding internist and member of the ACP/Rhode Island Chapter for long and sustained career service to patients, was given to a most deserving recipient, Dr. Herbert Rakatansky, Clinical Professor of Medicine, Brown University.

During lunch, a "Meet the Professor Session" was convened. Drs. Michael Goldstein, Edward Feller, Edward Lally, Thomas Wachtel, as well as the College representative, Dr. Zetterman, informally interacted with medical students, medical residents, and more senior physicians as they discussed several prepared cases in the respective specialties of psychiatry and behavioral medicine, gastroenterology, rheumatology, gerontology/general medicine and liver disease.

Afterward, a panel of Drs. Theresa Graves, Barbara Schepps, and Flora Treger discussed the management of breast masses, focusing on the management of problematic patients with breast disease. The audience participated in the discussion.

The day concluded with oral presentations of the remaining seven abstracts.

Once again, the meeting was felt to be a great success because of the quality of participants' work. The diversity of material presented, and the skills of the resident authors and their mentors, were obvious. It will be hard to improve on the format for next year.

Abbreviations Used

ACI	Adult Correctional Institution
AFB	Acid-fast bacilli
AMA	American Medical Association
ANA	Anti-nuclear antibodies
ARDS	Acute respiratory distress syndrome
AZT	Azidothymidine (Zidovidine)
BE	Barrett's Esophagus
BP	Blood Pressure
BUN	Blood urea nitrogen
CA	Carcinoma
CBC	Complete blood count
CHOP	Cyclophosphamide (cytoxan®), hydroxil daunoribucin (adriamycin®), vincristine (oncovin®), prednisone
CHOPE	Cyclophosphamide (cytoxan®), hydroxil daunoribucin (adriamycin®), vincristine (oncovin®), prednisone: VP-16 (etoposide®)
CLL	Chronic lymphocytic leukemia
CMV	Cytomegalovirus
CNS	Central nervous system
CT	Computed tomography
CXR	Chest x-ray
EA	Esophageal adenocarcinoma
ECG/EKG	Electrocardiogram
GERD	Gastrointestinal reflux disease
GI	Gastrointestinal
HIV	Human immunodeficiency virus
ICU	Intensive Care Unit
IVIG	Intravenous immunoglobulin
IVP	Intravenous pyelography
KUB	Kidney, ureter, bladder x-ray
KS	Kaposi's sarcoma
MAI	*Mycobacterium avium intracellulare*
MB	Myocardial bands
MEP	Maximum expiratory pressure
MIP	Maximum inspiratory pressure
MRSA	Methicillin resistant staphylococcus aureus
MVV	Maximum ventilatory volume
NIH	National Institutes of Health
NHL	NonHodgkin's lymphoma
N_0M_0	No lymph node involvement. No metastatic disease.
OR	Operating room
PANCA	Peri-nuclear anti-neutrophil cytoplasm antibody
PCNSL	Primary CNS lymphoma
PCP	*Pneumocystis carinii* pneumonia
PE	Physical examination
PD	Parkinson's disease
PFT	Pulmonary function tests
PRCA	Pure red rell aplasia
PV	Parvovirus
RT/CT	Radiotherapy/chemotherapy
SOB	Shortness of breath
SVT	Supraventricular tachycardia
TB	Tuberculosis
TMP/SMX	Trimethoprim sulfamethoxazole
VAMC	Veterans Administration Medical Center

1. An Unusual Presentation of Tuberculosis

Jennifer Clarke, MD
Rhode Island Hospital

The patient is a 66 year-old woman with a history of lower GI bleeding secondary to diverticulosis who was admitted to RI Hospital with a several week history of low grade fevers, weakness, increased abdominal girth and abdominal pain. She denied melena, diarrhea, hematochezia, or hematemesis. Physical exam was remarkable for a temperature of 101.5. Additionally, abdominal exam revealed left lower quadrant tenderness and a fluid wave consistent with ascites. Rectal exam was negative. Laboratory data were significant for a hemoglobin of 6.3 mg/dl. Chest xray showed reticular nodular scarring in both apices, consistent with old TB.

She was admitted with the diagnosis of diverticulitis and GI bleeding. She was started on Unasyn (ampicillin sulbactum). Over the next several days her abdominal girth increased and she remained intermittently febrile. Given these findings, an abdominal CT and paracentesis were performed. The CT showed bilateral cystic masses in the region of the ovaries, uterine enlargement, moderate ascites, omental cake and soft tissue masses anterior to the liver, felt to be highly suggestive of metastatic ovarian cancer. Ascites fluid was consistent with an exudate.

She was taken to the OR for debulking procedure for symptomatic relief of her abdominal pain. Path specimens revealed granulomatous disease which stained positive for AFB. The final diagnosis was disseminated abdominal tuberculosis.

Abdominal TB has become extremely uncommon in the United States secondary to antituberculosis chemotherapy and eradication of *M. bovis* by pasteurization of milk. It is encountered most often in immigrants, young adults and more often in females. It commonly presents with abdominal pain, anorexia and fever. It is not uncommon to present with an exudative ascites and/or a palpable abdominal mass. Most patients will have a positive tuberculin skin test or evidence of TB elsewhere in the body, particularly healed pulmonary lesions.

Clearly the diagnosis of abdominal TB should be entertained in the appropriate clinical setting. It is entirely curable if the diagnosis is made early enough and treatment is instituted early.

2. Adenovirus Epidemic

Susan Andrews, MD, and Walter Donat, MD
Rhode Island Hospital

This is a report of an epidemic of adenovirus causing respiratory failure in 5 institutionalized patients in July of 1995. There were 3 males and 2 females with ages ranging from 34 to 49. The chief complaints were fever, dyspnea, and cough. All the patients had schizophrenia. One had chronic renal failure (CRF), atrial fibrillation and hypertension. Another had adenoCA of the lung s/p pneumonectomy, diabetes, and mental retardation. Presenting symptoms included diarrhea, impaired mental status, and nausea. Laboratory findings included significant hypoxemia and diffuse infiltrates on chest xray.

All the patients were empirically started on broad spectrum antibiotics and required intubation for progressive hypoxemia. The courses were complicated by hypotension. Those requiring invasive hemodynamic monitoring showed high output states. Intensive care complications occurred, such as secondary infections with *aspergillus* and MRSA. All five patients tested positive for adenovirus. Four were eventually extubated and discharged. The patient with CRF failed to wean from the ventilator and he expired.

In children adenovirus is a common cause of pneumonia, bronchiolitis, and croup. In adults adenovirus pneumonia is described in military recruits, sporadic cases, and immunocompromised people. Despite these patients' initial multiorgan system failures, four survived without deficits. The literature notes a spectrum of disease from full recovery as seen in children to death in previously healthy people.

In the 1960's, a report summarized the study of adenovirus infections on military recruits. Common complaints were sore throat, cough, nasal symptoms, and headache, with signs of fever, rhinitis, and pharyngitis. These patients quickly recovered.[1] In 1967, JAMA published the first case of adenovirus causing a fatal pneumonia in a previously healthy adult.[2] In 1972, 3 previously healthy military recruits died of adenovirus-associated pneumonia. Each case included fever, respiratory symptoms, and radiological evidence of pneumonia with eventual multisystem organ failure.[3] Our cases had presentations similar to the cases in military recruits. They progressed rapidly to multiorgan system involvement and ARDS. Survival was attributed to prolonged supportive care in the ICU.

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3. Preoperative Cardiac Assessment in Peripheral Vascular Surgery: Review

Jimenez Carcamo, MD, W. Aude, MD, and Albert S. Most, MD
Rhode Island Hospital

The purpose of this abstract was to review preoperative cardiac assessment in patients undergoing major vascular surgery. The data presented was based on a computerized search of the current literature. Ten major studies were selected to identify the most relevant cardiac risk factors for perioperative complications. The roles of preoperative electrocardiography, exercise stress electrocardiography, stress echocardiography, thalium stress testing and angiography relevant to this population are present. Risk reduction techniques are also shown in this comprehensive review of preoperative cardiac assessment.

In the vascular patients, symptoms may underestimate the degree of risk, since, as shown by Hetzer et al, the prevalence of significant asymptomatic coronary artery is very high. Goldman cardiac risk factors, Detsky cardiac risk index and Eagle vascular surgery risk markers are the best known predictors of postoperative cardiac complications. However, the majority of patients referred for vascular surgery fall in an intermediate risk category by clinical criteria. Dypiridamole thallium and dobutamine stress echocardiography are the most suitable tests to risk-stratify these patients. Vascular patients generally have poor physical condition, symptoms of claudication and baseline electrocardiogram abnormalities. A positive stress test or unstable angina by clinical evaluation is an indication for preoperative coronary angiography.

Once risk-stratification is achieved, operative risk reduction should be planned. This includes coronary revascularization, invasive monitoring, antianginal medication and alternative surgical techniques.

Based on the data reviewed, we propose an algorithm for the risk stratification of patients undergoing vascular surgery.

4. Former Prisoners' Views on Mandatory HIV Testing During Incarceration

B. Ramratnam (Associate), MD, G. Tsoulfas, MD, A. Parikh, MD, J.D. Rich, MD, MPH and T.P. Flanigan, MD

The Miriam Hospital

Most prison inmates are young and poor with a history of substance abuse that places them at high risk for HIV infection. HIV seroprevalence in US prisons has ranged from 2.1% to 14.7%. Mandatory testing of prisoners for HIV has been recommended by the AMA and at present 10 states, including Rhode Island, and the Federal Prison System have mandatory testing procedures. Recent reports on prisoner acceptance of HIV testing have been confined to prison systems with voluntary programs. No reports have examined former prisoners' views on mandatory HIV testing.

130 former prisoners who underwent mandatory HIV testing at the RI Adult Correctional Institution (ACI) were surveyed at 2 sites: a methadone maintenance program and a health center for HIV (+) and high risk individuals. During a 5 minute anonymous interview they were asked: "Should HIV testing be voluntary or mandatory in prison" and "How do you feel about mandatory HIV testing - good, bad, no opinion." The respondents' age, sex and HIV status were noted.

Of 130 individuals, 54 men and 76 women, there were 80 Whites, 32 African-Americans, 15 Latinos, and 3 Native Americans. 65/130 (50%) were HIV (+). 48/465 (72%) of HIV (+) and 50/61 (88%) of HIV (-) individuals felt that HIV testing should be mandatory for all prisoners. When individuals were asked how they felt about mandatory HIV testing in prison, 101/130 (78%) felt good, 21/130 (16%) felt bad and 8/130 (6%) had no opinion. Individuals approved of mandatory testing because they felt that HIV (+) persons should know their diagnosis so that they could receive appropriate medical care, plan for the future, and modify behavior to lessen the chance of spread to their partners. Reasons for disagreeing with mandatory testing centered around the coercive nature of testing, skepticism regarding confidentiality of test results and doubts regarding the quality of medical care in prison.

It is surprising that 80% approved of mandatory testing. The survey's results should not be interpreted as blanket approval of the principle of mandatory testing but affirmation of the HIV care program in the ACI. Core components of the program include: 1. HIV (+) individuals are given extensive post test counseling and support. 2. HIV status is known only by members of the medical team and not by correctional officers or administrators. 3. HIV (+) prisoners are not segregated. 4. Medical care is provided by dedicated nurses and physicians with training in HIV/AIDS. 5. Discharge planning efforts are made to link individuals with community based drug and alcohol rehabilitation programs and HIV support groups upon release.

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5. A Case Series of NonHodgkin's Lymphoma (NHL) in Patients with AIDS

Hueiguo G. Lin, MD. Timothy Flanigan, MD, and Anthony Mega, MD

The Miriam Hospital

NHL will occur in 5-10% of the AIDS population. Although extra CNS NHL is recognized as chemotherapy responsive, a recent NIH survey showed significant undertreatment of primary CNS lymphoma (PCNSL) in AIDS patients due to the physician's conviction of ineffectiveness of therapy.

Seven cases of AIDS-related lymphoma from 1990 to 1995 at the Miriam Hospital were reviewed. Patient age ranged from 28 to 41, 3/7 were females, 2/7 patients presented with PCNSL. The pathology was high grade diffuse large cell lymphoma except one case of diffuse mixed cell lymphoma. All five patients with extra CNS NHL had CD4 counts ranging from 20-5000/ul had been treated with multiagent chemotherapy (CHOP or CHOPE) and had attained complete remission. One female patient with CD4<50 with mediastinal mixed cell lymphoma after four cycles of CHOP achieved a two years disease free survival. The two other patients with a CD4>400/ul recently treated with CHOPE are currently disease free for 3 months. The remaining two patients died at three months and eight months due to CMV pneumonia and AIDS wasting syndrome respectively after completion of the chemotherapy. Extra CNS AIDS NHL is responsive to chemotherapy. In our small series, the complete response rate was 100% and fatalities were due to opportunistic infection instead of tumor progression.

Management of PCNSL is controversial. Both patients with the primary CNS lymphoma were managed with dexamethasone alone and died with rapid progression in a period of 2-4 months after diagnosis. The reported median survival of PCNSL treated with steroid and whole brain radiation is 2.6 months. A small series at Cornell revealed that chemotherapy plus whole brain radiation could lead to complete remission in PCNSL in 86%, but survival in complete responders was compromised with fatal opportunistic infections. Therefore, chemotherapy and effective opportunistic infection control should ultimately improve the survival of patients with AIDS related lymphomas.

6. Myopericarditis Associated with *Campylobacter jejuni*

Arthur P. Williams, MD, Helena Kwakwa, MD, and David Marcoux, MD
The Miriam Hospital

Campylobacter jejuni is a frequent cause of enteric infections in the United States. A typical presentation involves a history of ingestion of inadequately cooked poultry followed by fever, gastrointestinal symptoms, and headache. Examination of stool often reveals small, curved, motile, gram negative rods. *C. jejuni* infections can occasionally be complicated by more serious postinfectious entities such as Guillain-Barre syndrome, reactive arthritis and rarely carditis.

A 37 year-old man presented to the hospital, two days after eating undercooked chicken, with frequent episodes of nonbloody diarrhea and mild abdominal pain. On examination, the patient was febrile to 38.5 C, orthostatic and tachycardic. The heart and abdominal exams were normal. The white blood count was 13,600 with 8% bands. On the first hospital day, the patient developed two hours of substernal chest pain which had a respirophasic component and was relieved by a non-steroidal medication. An EKG obtained showed inferior and precordial ST segment elevation. Serial EKG's demonstrated normalization of the ST segments with new inversion of the precordial T waves. Creatinine phosphokinase rose to a peak of 760 I.U. with a MB index of 4.8% over 24 hours. Echocardiogram and stress thallium tests were normal. Stool cultures were positive for *C. jejuni*. Viral titers for Cocksackie A and B, echovirus, and *B. burgdorfi* were negative. Convalescent serium antibodies to *C. jejuni* were elevated.

Myopericarditis is difficult to distinguish from acute myocardial infarction and is often the result of an infectious agent. Salmonella, shigella, and *Y. Enterocolitica* have been associated with carditis. However, there are only a few published reports implicating *C. jejuni*. This case illustrates an example of myopericarditis associated with *C. jejuni* masquerading as acute myocardial infarction.

7. Natural Course of *Aspergillus fumigatus* Experimental Endocarditis in Rabbits

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Systemic aspergillosis has increased in frequency as immunocompromised patients live longer; in particular patients with AIDS, hematologic malignancies and solid organ or bone marrow transplantation are at risk for invasive aspergillosis. Current treatment is inadequate to control the infection and the mortality of invasive aspergillosis is still high.

A reliable and reproducible experimental model for the *in vivo* study of systemic *Aspergillus* is needed. We studied the natural course of *Aspergillus fumigatus* in the Freeman and Beeson experimental animal model. Non-bacterial thrombotic endocarditis was induced in the aortic valve of New Zealand rabbits and three days later animals were challenged with an inoculum of 10^7 spores of *Aspergillus fumigatus.* At selective time points through a seven day time period the sixteen rabbits of our experiment were sacrificed and the aortic vegetations were quantitatively cultured. Endocarditis developed in all animals. Cumulative mortality progressively increased from 20% after the first day, to 63% on the fourth day and to 80% on day 7. Quantitatively cultures revealed a progressive rise of fungal concentrations in the vegetations. A peak at day four was noted.

Experimental *Aspergillus fumigatus* endocarditis in rabbits can be a useful model for the study of prophylactic and therapeutic efficacy of antifungals. Further *in vivo* and *in vitro* trials are essential to decrease the morbidity associated with this infection.

* * *

8. L-Dopa Induced Respiratory Dysfunction

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Memorial Hospital of Rhode Island

Parkinson's disease (PD), characterized by degeneration of the dopaminergic nigrostriatal pathway, causes deterioration. Fortunately levodopa is an effective therapy but there are significant side effects. We present a patient whose adverse reaction made her noncompliant with therapy.

The patient is a 69 year old woman with a history of mild asthma and PD for 5 years, L-Dopa was prescribed. The patient stopped taking her medication because it made her "short of breath" (SOB). She stated that within 30-60 minutes of taking her dose her respirations became shallow and irregular, and that this effect resolved 2 to 4 hours after the dose. When she stopped taking her L-Dopa, she had only symptoms of PD, breathing was normal. On exam, respirations were 18 per minute and regular, her lungs were clear, she had resting tremors and a slow gait. Her PFTs showed moderate obstructive dysfunction and reduced MVV, MIP, and MEP. Baseline respiratory muscle plethysmography (off L-Dopa) showed a normal regular respiratory pattern, but 30 minutes after taking L-Dopa the tracing disclosed an irregular pattern of breath amplitude and rate. During this time the patient was SOB and had neck and shoulder muscle dyskinesia. This effect lasted about 2 hours.

L-Dopa induced dyskinesias are characterized by choreoathetoid movements similar to those seen in Huntington's and Senile Chorea. It affects up to 50% of patients on L-Dopa. Movements involving the face, mouth, limbs are well described. Few reports describe respiratory dyskinesia with L-Dopa which may be present alone or with other dyskinesias. It has been postulated to be a chorea of the respiratory muscles, others propose a form of denervation hypersensitivity of altered dopaminergic cells in respiratory control areas. In many patients the effect seems to be dose-related and adjusting the dose of L-Dopa can resolve the symptoms. Others respond to a dopa antagonist like tiapride.

Recognizing this adverse reaction can spare these patients many unnecessary tests, improve compliance, and therefore, better their symptoms of PD.

9. Abdominal Aortic Aneurysm Masquerading as Renal Colic

Julie Davis, MD, and Robert Crausman, MD

Memorial Hospital of Rhode Island

Abdominal aortic aneurysms are common in aging males at risk for atherosclerotic disease. They are often asymptomatic and incidental but can be associated with significant morbidity. When symptomatic, they can mimic many intra-abdominal diseases. Here we present a case of an abdominal aortic aneurysm that resembled renal colic.

A 70 year old man with a history of hypercholesterolemia and nephrolithiasis presented to the emergency room with the acute onset of right sided back and flank pain similar to his renal colic 30 years ago. His physical exam was unremarkable. A urinalysis was negative. Electrolytes, BUN, creatinine, CBC, and hepatic enzymes were all normal. He was thought to have renal colic, was given IV fluids, narcotics and sent home.

He returned several hours later with bilateral flank pain. He also felt nauseated and vomited once in the emergency room. His vital signs were a temperature of 100.7, pulse of 95, and blood pressure of 164/96. Examination revealed no abdominal tenderness or masses, no costovertebral angle tenderness or ecchymosis, and heme negative stool. Lower extremity pulses were weak but palpable. Repeat urinalysis contained 3-5 white blood cells, 2-5 red blood cells, 2+ calcium oxylate crystals and 3+ amorphous urates. A KUB suggested no stones and an indistinct right psoas margin, and IVP also indicated no stone or obstruction. However, on closer examination, the IVP demonstrated superolateral displacement of the right kidney and a bulging right psoas shadow. A retroperitoneal hemorrhage was suspected, and on abdominal CT scan he was found to have a 9 cm ruptured abdominal aortic aneurysm. He was taken to surgery for repair and is currently recovering and doing well.

This case demonstrates an atypical presentation of a potential surgical catastrophe. This patient appeared relatively stable, and the fully appropriate work-up and treatment for renal colic might have been continued if not for the subtle findings on IVP. In this era of cost containment, one cannot feasibly perform a CT scan to work up all cases of back and abdominal pain. Therefore, no matter how straight forward a case appears, one must maintain a critical eye to identify other potentially life-threatening diagnoses when interpreting diagnostic tests.

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10. 19th Century Medicine: Tachycardia Treated with Bugle Weed

David A. Lyon, DO, D. Hom, and Cynthia Alves, MD
Roger Williams Medical Center

A 78 year-old pastor with a history of hypertension and supraventricular tachycardia (SVT) presented for evaluation of new onset chest discomfort. He has no other significant past medical history. He takes Verapamil and digoxin daily. The patient continued to have occasional episodes of rapid heart action which he treats acutely with Bugle Weed. He feels that Bugle Weed controls his heart and refuses to stop using it. The chest discomfort was not entirely typical of angina. PE was normal except for a pulse of 45. The patient was admitted for observation. There was no evidence of myocardial injury by ECG or enzymes. He exercised on a treadmill to a peak heart rate of 98, without chest discomfort, but thallium images revealed inferolateral ischemia. He had no recurrent chest discomfort, declined cardiac catheterization and was discharged on Verapamil and prn Bugle Weed.

Bugle Weed (*Lycopus virginicus)* is a medicinal plant indigenous to North America where it ranges from Florida to British Columbia. It blossoms from July to September. It was first used as a medicine in Europe as a styptic to stop bleeding such as nose bleeds, minor wounds, and menorrhagia. It was also found to act like digitalis by lowering the BP and pulse without producing "bad effects." Dr. Rainesque (Am Med Assoc 1849, 902) highly valued its general properties and its means of producing diaphoresis without debility. *Lycopus* was dismissed from the *U.S. Pharmacopoeia* at its last revision but is still used today by herbalists and homeopaths. It is listed in Beoricke's *Materia Medica* 1994 edition. Approximately 1/3 of U.S. adults use alternative therapies spending about $14 billion per year, $10 billion of which is out-of-pocket money. The NIH Office of Alternative Medicine opened in the early 1990's to evaluate the efficacy of certain non-traditional treatments. This case is a good example of how conventional doctors will be faced with an increasing patient population using alternative medicines.

11. *Pneumocystis carinii* Pneumonia: Variations in Presentation and Response To Therapy Based on Host Factors

Mary B. Callahan, DO, and Joseph V. Meharg, MD
Roger Williams General Hospital

An 80 year-old female with known Wegeners granulomatosis (+P-ANCA; -ANA) was admitted with nonproductive cough, fever, chills and dyspnea. Medications at the time of admission included cytoxan and prednisone. Initial chest film demonstrated minimal air space disease, more prominent on CT scan, she was placed on broad spectrum antibiotics for a community acquired pneumonia (PCP). Her HIV serology was negative, and she was started on trimethoprim/sulfamethoxazole (TMP/SMX 20 mg/kg/day) then discharged home for 21 days of treatment. One week following discharge she was readmitted for worsening symptoms and CXR. Open lung biopsy was diagnostic for PCP, without signs of vaculitis. Thrombocytopenia developed necessitating a change to intravenous pentamidine (4 mg/kg/day). On hospital day 14 she was extubated as per her prior wishes.

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PCP is an opportunistic infection occurring in immunocompromised hosts with and without AIDS. Review of the literature demonstrates significant differences in presentation, degree of illness and outcome between HIV positive and negative groups.

	HIV	non HIV
Duration of Symptoms	28 days*	5 days
PaO2	69*	52
Respiratory Rate	23*	30
Mortality	10-20%	32-50%

*p<0.001

With the increased use of immunosuppressive therapies for diseases such as the vasculitides and connective tissue disorders, physicians are more likely to encounter these patients. In this presentation, we will review the data on PCP in the non-AIDS population. We speculate that the response to therapy may be different in the non-AIDS population and caution physicians to be aware that there are currently no controlled therapeutic trials or treatment recommendations for PCP in non-AIDS patients.

12. Surveillance of Patients with Barrett's Esophagus

Songul Atay, MD, and Harlan Rich, MD
Roger Williams Medical Center

Barrett's esophagus (BE), columnar metaplasia of the distal esophagus, affects nearly 700,000 people in the U.S. and carries a 30-125 times greater risk of esophageal adenocarcinoma (EA) than that of the general population. Because EA arises from dysplastic Barrett's mucosa in an asymptomatic period of 4.5 years and has a poor prognosis once the symptoms develop, patients with BE might benefit from periodic endoscopic surveillance with biopsy.

We reviewed 137 patients who presented with symptoms related to upper GI and had endoscopy between 1989-1995 at the Providence VAMC. Initially, 121 patients had BE (group 1) and 16 had EA (group 2). Of the 121 patients, 18 developed dysplasia and 4 progressed to EA (group 1A). Average age at presentation was 62.82 for group 1A and 62.19 for group 2. History of smoking and/or alcohol was positive in 25% of group 1A and 100% of group 2. Initial symptoms were GERD in 50% of group 1A and dysphagia in 40% of group 2, with the remaining patients having vague or no symptoms. All patients in group 1A had stage NoMo disease, whereas 70% of the group 2 presented with node involvement and/or metastases. All patients in group 1A were treated with surgery. 25% of group 2 patients had surgery, and 75% had RT/CT. Average survival was 37.56 months (s.d.=16.79) for group 1A and 14.98 months (s.d.=13.05) for group 2. All patients in group 1A and 12.5% in group 2 are alive to date, with the patients in group 1A being asymptomatic and those in group 2 having to undergo RT CT. The patients whom we did not have sufficient data for at the present time were excluded from this review, but will be included in the final report.

Our review suggests that endoscopic surveillance markedly increases life expectancy and quality adjusted life expectancy by identifying high-grade dysplasia, by measuring its extent and by detecting early invasive carcinoma. Since it is unknown if and when it will progress to carcinoma, patients with proven high grade dysplasia should be followed closely and treated surgically even if proof of malignancy is questionable. Dysphagia, weight loss and pain, are seen later in the disease process and are ominous signs for survival. Whether all patients with BE or only those with dysplastic changes should be monitored is controversial. Although the cost-benefit ratio of routine endoscopic surveillance of BE may be debated, we believe that it is the most definitive study available and is justified until more definitive and cost-effective studies are conducted.

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13. HIV Associated Pure Red Cell Aplasia (PRCA): A Diagnostic and Therapeutic Dilemma

Rashed Nizam, MD. and Nancy Freeman, MD, FACP
Veterans Administration Medical Center

A 33 year-old HIV positive bisexual Hispanic male on AZT, Dapsone, rifabutin, and a gancyclovir intraocular implant (all for > 1 yr) with cryptosporidium, MAI in the stool, CMV retinitis, oral thrush, Kaposi's sarcoma (KS), and recurrent sinusitis developed transfusion dependent anemia in 5/95. He had no hemolysis and a reticulocyte count of 0%. His smear showed hypochromic microcytic red cells, and the marrow <1% erythroblasts, 2+ iron, and myeloid dysplasia consistent with PRCA and HIV. A work up for PRCA revealed stable KS, a marrow culture positive for MAI (clarithromycin added), a negative chest CT for thymoma, serologies negative for mononucleosis, hepatitis A, B, and C, acute CMV titers positive, and a parvovirus B19 (PV) IgG, IgM negative, DNA positive, indicating a chronic infection. The AZT was discontinued, and intravenous immunoglobulin (IVIG) was considered. PRCA is an unusual syndrome characterized by a severe anemia, <1% reticulocytes, and <1% erythroblasts in the marrow. Acquired PRCA may be idiopathic, immune, or associated with thymoma or other malignancies (KS, lymphoma), infections (PV, hepatitis, mononucleosis, CMV, HIV), nutritional deficiencies, inflammation, and drugs (AZT, dapsone). The proposed pathophysiologies involve IgG mediated inhibition of erythropoietic precursors (50% of cases), T cell mediated (CLL), and PV toxicity to erythroid precursors. Treatment includes supportive care (transfusions and Desferal @ = $600/month), therapy of the underlying condition, steroids, immunosuppressive agents, splenectomy, and now IVIG @ $7500/month, which may supply antibodies to neutralize the cytotoxic IgG or PV. The relapse rate is 80% in 24 months with 12% spontaneous remission after 5 months to 14 years. PRCA in HIV patients has only recently been described in scattered reports, one showing a permanent response to AZT, and another to its discontinuation. Most cases of PRCA (HIV, PV, or not) responded only transiently to IVIG, necessitating monthly therapy. PRCA in HIV may result from an array of etiologies; although one might offer a single course of IVIG with hopes of a permanent response, cost benefit issues should be considered, and other therapeutic modalities attempted, prior to embarking on long term costly IVIG.

Indeterminate Results of HIV Testing: Explanation and Clinical Management

Bethany C. Elliot, BA, Maya Rogers, MD, and Josiah D. Rich, MD, MPH

Of the total number of HIV tests done in Rhode Island, a significant amount (possibly up to 10%) will be judged indeterminate.[1] There is much confusion about the interpretation of an indeterminate HIV test result and how best to evaluate and counsel patients. This article seeks to clarify the confusion and provide guidelines for dealing with ambiguous results.

Because of the tremendous public health and potential individual benefit from early detection and treatment of HIV, it is imperative that indeterminate results be handled appropriately. To understand the meaning of an indeterminate HIV test, it is necessary to understand how an HIV test is performed. HIV serum testing measures the presence of antibodies that bind to HIV particles, first by enzyme linked immunosorbent assay (ELISA or EIA) and then, if positive, by Western Blot. Serum is first tested by ELISA, a very sensitive test which detects the presence of antibodies that bind to HIV. A small amount of serum is placed in a test tube coated with HIV antigen. If the serum contains antibodies to HIV, they will bind to the HIV particles in the test tube and the solution will change color as the result of a chemical reaction occurring between an enzyme and a substrate.

If the ELISA is found to be positive it is repeated. If found to be reactive again, a Western Blot is performed. The HIV particle is composed of three main parts: GAG (inside the virus), ENV (the outside envelope of the virus), and POL (the polymerase portion of the virus) (Figure 1). A Western Blot kit contains paper strips with HIV particles bound to it, separated by size into the different viral proteins, each fitting into one of the three categories (Figure 2). Serum is placed on the strips. If the serum contains antibodies to the HIV virus the bands will become visible. A positive Western Blot, as determined by CDC criteria, is defined as the presence of antibodies against two proteins: one from the inside of the virus (GAG), one from the outside (ENV). For example, if bands p24 (from the GAG portion) and gp41 (from the ENV portion) light up, the blot is positive.Any combination of bands that do not fit the criteria for positive are considered indeterminate. A negative result is defined as the absence of any reactive bands.[2] At the Rhode Island Department of Health, immunofluorescence, another test which is similar to an ELISA but uses a fluorescent microscope to detect the HIV antibodies, is also performed in the event of an indeterminate or a positive Western Blot.

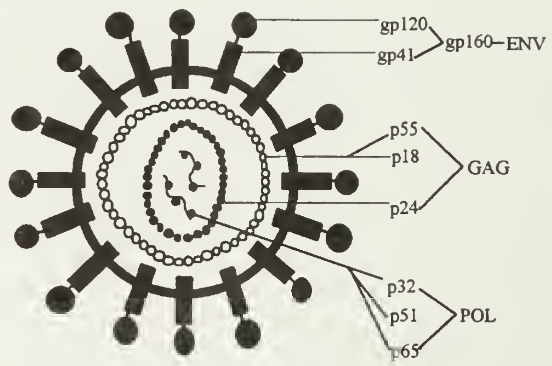

Figure 1.
The structure of HIV separated into the three categories: GAG, ENV and POL.

Abbreviations Used:

CDC	Centers for Disease Control and Prevention
DNA	Deoxyribonucleic acid
ELISA	Enzyme-linked immunosorbent assay
ENV	Envelope segment of HIV
GAG	Interior segment of HIV
HIV	Human immunodeficiency virus
PCP	*Pneumocystis carinii* pneumonia
PCR	Polymerase chain reaction
POL	Polymerase segment of HIV

An indeterminate result of a Western Blot could mean three things. First, the person was recently infected and is in the process of developing HIV antibodies. This is commonly referred to as the window period. In this case, the patient has not yet developed sufficient HIV antibodies to be reactive with all the different viral proteins. Second, the person could produce antibodies that coincidentally cross-react. This can occur when a person has HIV-2, a different strain of HIV that is rare in the United States, or it can rarely occur in people who have recently had a flu shot or women who have had multiple births.[3] Third, the person could be in an advanced stage of HIV infection when antibody levels are declining. They would likely be evidently ill. However, this is extremely unlikely with the improved Western Blot tests.[4]

In the case of primary HIV infection, one must look for clinical signs of infection and at the case history for possible risk factors. The severity of symptoms present during the time of infection ranges from acute mononucleosis-like viral syndrome (40%-60% of seroconverters) to patients who are asymptomatic.[4] If symptoms are present, they often occur within 1 to 6 weeks of infection and last less than a week. Common symptoms can include fever, lymphadenopathy, rash (often non-pruritic erythematous and macular), headache, muscle aches, sore throat, and retroorbital pain. Some patients have transient, severe immunosuppression-associated, and potentially life-threatening, opportunistic

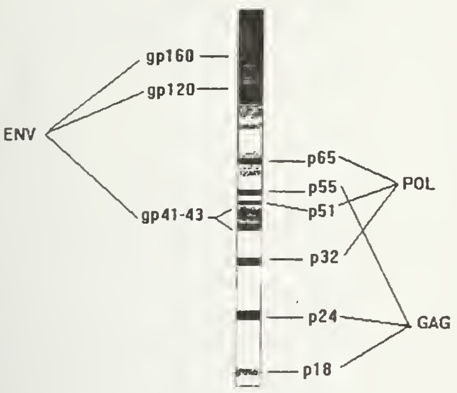

Figure 2.
A Western Blot strip with different viral proteins separated into the three categories: GAG, ENV and POL.

infections including *Pneumocystis carinii* pneumonia (PCP), oral candidiasis, ulcerations of the esophagus and anal canal, acute central nervous system disorders, diarrhea and other gastrointestinal complaints.[4] Most symptomatic patients seek health care and are diagnosed with a non-specific "viral syndrome" or aseptic meningitis. These symptoms are often not recognized or diagnosed as symptoms of acute HIV infection.

Previous studies on indeterminate Western Blots have discovered no definitive trends which predict whether a certain band pattern will seroconvert. A relative consensus has been reached that Western Blot patterns characterized by the absence of p24 and *env* products are almost certainly not due to HIV infection. In fact, the presence of a p24 band on the Western Blot may signal a possible seroconversion and should be aggressively followed for repeat testing.[5,6] But these results vary considerably depending on the sample group. The rate of seroconversion among indeterminates depends upon the likelihood of HIV exposure and has been reported in the range of 3%-5% among low-risk individuals and up to18% among high-risk individuals.[7,8,9] We have seen as high as a 90% seroconversion rate in a large high-risk group of prison inmates. A history of risk behavior within the last 3-6 months makes it more likely that the indeterminate could signify the beginning of seroconversion.

In the event of an indeterminate, the Rhode Island Department of Health advises that an ELISA and Western Blot be repeated in thirty days. On average, people infected with HIV seroconvert (create a significant amount of anti-HIV antibodies) within 3-6 months after infection.[4] Therefore, if repeat HIV tests are done before possible seroconversion, they will continue to be indeterminate on Western Blot. This can be frustrating for the patient.

More sensitive adjunctive tests may be done, which include the p24 antigen test, PCR (polymerase chain reaction) or viral load (quantitative PCR or b-DNA testing), which can detect the virus before the ELISA or Western Blot become positive. Several studies suggest that measures of HIV viral load are sensitive and specific.[10] These new tests that measure viral load are likely to make the evaluation of indeterminate Western Blots simpler. However, the cost (around $200 for PCR) is not yet comparable to an ELISA and/or Western Blot (around $60).

> *Because of the tremendous public health and potential individual benefit from early detection and treatment of HIV, it is imperative that indeterminate results be handled appropriately.*

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Advantages for early diagnosis include early treatment and prevention of further transmission. Studies suggest that early intervention with antiretroviral drugs will improve CD4 count levels and may have a dramatic effect on long-term survival.[11] Also, early detection can ease contact tracing (searching for people who may have been in contact with the infected person and are possibly at risk).

In the meantime, the clinician should inquire about a history of prior risk behaviors and monitor the patient for acute viral symptoms. A repeat ELISA and Western Blot should be performed and, ideally, an HIV viral load. The patient should be counseled to abstain from sex or observe safe sex techniques (latex condoms) and, in the case of injection drug use, refrain from sharing injection equipment. In the setting of a true seroconversion the patients are potentially very infectious in the first 3 months of infection. Improved awareness of acute HIV infection and the appropriate interpretation of indeterminate HIV antibody tests will hopefully lead to early identification of HIV infection and improved HIV-related counseling.

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Point of View: HIV and Competitive Athletics – Assessing the Real Risk of Infection

Alexander A. Feller, BA, and Timothy P. Flanigan, MD

Magic Johnson's November 7, 1991 announcement that he had become infected with the human-immunodeficiency virus (HIV) ushered in the public marriage between AIDS and sports. It has been a rocky relationship full of innuendo, misconceptions, and legitimate concern. The recent positive HIV test of boxer Tommy Morrison and Magic's return to professional basketball have amplified speculation about the risk of contracting HIV in competition. Yet, despite increased publicity and scientific evidence, both the public and those involved directly in competitive athletics often appear ignorant of the actual risk of transmission of HIV in competition and fear that exercise will accelerate the course of HIV infection in the immunocompromised individual. Rational scientific inquiry, not alarm, should guide the discussion of HIV and the competitive athlete.

The actual number of HIV-positive athletes is probably quite small. In a year-long survey of National Collegiate Athletic Association (NCAA) member institutions, only 12 of the 548 responding schools reported having HIV-positive or AIDS-diagnosed athletes.[1] Since only 22 schools administer "routine" HIV testing and only 2 require mandatory testing of athletes, determination of the number of HIV-infected collegiate athletes is not currently feasible. An examination of other groups at similar risk for contracting HIV gives perhaps the best approximation of the number of HIV-infected athletes. The prevalence of HIV among university students has been estimated at 0.2% while the United States armed forces reports an HIV infection rate of 0.14%.[2] These groups consist of men and women likely to approximate the AIDS risk of those competing in high school, intercollegiate, professional, and international sporting events; both have prevalence rates indicative of groups not considered at high risk of HIV infection.

Abbreviations Used:

AIDS	Acquired immune deficiency syndrome
HIV	Human immunodeficiency virus
NCAA	National Collegiate Athletic Association

If the number of HIV-infected athletes competing seems minute, the risk of an actual transmission via competitive athletics appears even smaller. Laboratory testing has indicated that HIV is not present in "natural" sweat and has not been transmitted via saliva, tears or urine.[3] No transmission in an athletic contest has been verified scientifically. Physicians at an infectious disease unit in Varese, Italy, reported an HIV transmission in a soccer match after a head-to-head collision between a seronegative player and an HIV-positive IV drug user, but they could not confirm that the player had not been infected by a work-related incident at his job at a drug rehabilitation center.[4] "Sportlike" transmissions, however, have been documented. The Centers for Disease Control verified the HIV transmission during two separate fist fights, one of which involved a nasal hemorrhage that bled into an open cut on the forehead of a previously seronegative male.[5] The possibility of HIV transmission in the athletic setting via blood contact is, therefore, a real one, albeit rare. One study, quantifying the frequency of bleeding injuries during an entire National Football League regular season, assessing the prevalence of HIV among college men, and the risk of HIV transmission of exposed health care workers, estimated the overall risk of HIV transmission in professional football to be 1 per 85 million game contacts.[6]

Competitors who are legitimately concerned about contraction of HIV through athletics should worry more about off-field behavior. For example, intramuscular injection of anabolic steroids represents another poorly publicized potential risk factor associated with sports. Estimates of steroid use among college and high school athletes vary; one study of 1,010 college men estimated steroid use at between 2 and 20%. Although only one reported instance exists of HIV transmitted to a body-builder by sharing contaminated needles for anabolic steroid injection, an estimate that 38% of steroid users employ injectable steroids suggests that contaminated needles are a potential source of future HIV infection among athletes.[7,8]

The real off-field and out-of-ring risk of HIV infection has not stopped some state athletic commissions from requiring mandatory HIV testing of all boxers. Since instituting this policy, Nevada has tested 2,100 boxers for HIV; only two men have tested HIV positive.

Some have also attempted to prohibit HIV-infected athletes from competing based on the concern that the rigors of athletic activity may damage their health. In fact, evidence suggests that moderate exercise by infected athletes enhances immune function, raising the level of CD4 cells, and reducing the stress and depression associated with HIV.[9] Aerobic activity may also improve muscle function and cardiorespiratory performance. Little data exists on the effects of high intensity exercise on the HIV-infected individual; however, as Magic Johnson's smooth comeback illustrates, the HIV-infected athlete can withstand the physical and mental pressures of elite competition.

HIV is a deadly virus and should be treated with respect, not unwarranted fear. The blood of every athlete in so-called "combative sports" must be treated as a potential vector for infection. Most athletic commissions sanctioning boxing events require referees and handlers to wear protective gloves and abide by so-called "universal" precautions. Such precautions involve pre-dressing any existing surface lesions and skin abrasions before competition, cleaning any bleeding wound sustained during competition with an appropriate antiseptic and bandage, changing any uniforms saturated with blood, as well as decontaminating surfaces on which blood has been spilled. These guidelines also counsel the infected athlete to seek medical advice before deciding to compete, but uphold the athlete's right to confidentiality and declare mandatory testing unwarranted as a public health measure. Universal precaution practices have been adopted by governing bodies such as the NCAA, the American Academy of Pediatrics, and the World Health Organization to prevent the transmission of blood-borne pathogens, such as hepatitis B and HIV from athlete to athlete and athlete to trainer.

> *Rational scientific inquiry, not alarm, should guide the discussion of HIV and the competitive athlete.*

When exposure to blood is commonplace as in professional boxing, the appropriate public health response should be to institute safeguards decreasing the likelihood of blood exposure without requiring universal HIV testing. The headgear, heavier gloves, shorter fights, and rigorous policing of boxers' safety which prevail in amateur boxing, provide a blueprint for reducing the risk of blood-borne exposure. Such safety guidelines would also decrease a more worrisome aspect of professional boxing: the risk of head injury leading to cerebral hemorrhage, chronic brain damage or death.

Given the shaky public health imperative to test all boxers for HIV, these mandatory HIV tests also highlight some contentious right-to-privacy and discrimination issues. Legally, those deemed at low risk of contracting HIV cannot be subjected to mandatory testing without proof of the necessity of protecting the safety of the infected athlete and other competitors. Furthermore, the Americans with Disabilities Act of 1990 guards expressly against "unjustified discrimination" against people with HIV or other disabling conditions. Mandatory HIV testing in professional boxing is an emotional response that fails to address the more important risks inherent in the sport and perhaps violates the legal rights of the participants.

Prevention of HIV in the sports arena should focus on precautions to prevent exposure to potentially infected blood, not on capricious regulations for mandatory HIV testing. A negative

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HIV test may only provide false security because the test may be falsely negative during the "window" period of early HIV infection. The self-reported risky lifestyles of Tommy Morrison and Magic Johnson provide a more accurate scenario for future HIV infection among athletes. Evidence suggests that athletes may engage in a significantly higher level of "risky" lifestyle behaviors compared to non-athletic controls.[10] The risk factors include amount of alcohol consumed, driving an automobile while under the influence of alcohol, avoidance of contraceptive use, number of sexual partners, and history of sexually transmitted diseases. This association highlights the reality that risk of HIV infection is much more likely to be the result of off-field behavior than the extremely low risk of contracting HIV in formal competition. Dissemination of information about high-risk off-field behavior and common sense implementation of universal precautions is the appropriate way to decrease the already low risk of HIV transmission during sporting events.

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Physicians Newly Licensed in Rhode Island During 1995

Nikki Deary, Milton W. Hamolsky, MD, and Stanley M. Aronson, MD, MPH

The Rhode Island Board of Medical Licensure and Discipline, at yearly intervals, publishes a brief demographic description of those physicians who have been newly licensed in the state during the preceding year. The current profile detailing the new medical licensees of 1995 represents the sixth such report to appear in this journal.[1-5]

During 1995, 264 allopathic physicians were granted licenses to practice medicine in Rhode Island. This was the largest yearly number of licenses granted in the last four decades and represents an 8% augmentation of the state's medical profession.

GENDER AND AGE

Table 1 summarizes the age and gender distribution of these 264 physicians, comparing them to profiles from the three preceding years. While there are yearly fluctuations, women physicians continue to constitute about one-third of all newly licensed physicians. The average age of newly licensed women physicians is 34.5 years; of newly licensed males, 37.6 years. A consistent gender difference of about two years in average age has also characterized the new physicians of 1992, 1993 and 1994, largely because of the weighted presence of newly licensed physicians older than 50 years, virtually all of whom had been male. For example, in the 1995 cadre 3.3% of the newly licensed males, but none of the newly licensed females, were age 61 or older. Many of these older physicians entering the state were recruited to work as administrators of health care organizations rather than to enter the clinical practice of medicine. Some, too, have sought licenses in order to establish satellite offices in Rhode Island while maintaining their principal professional offices in Massachusetts or Connecticut.

Some of the new licensees are still in residency training or subspecialty fellowship. They had sought licensure at this time either because their supervised training may involve them in a limited form of private practice or because they had been granted permission to work as substitute physicians ["moonlighting"] when not formally on duty.

PLACES OF BIRTH

The places of birth of the newly licensed physicians are summarized in Table 2. Over half [53.4%] were born either in New England or in the middle Atlantic states. In these yearly compilations, Massachusetts or New York-

Table 1

Physicians Newly Licensed in Rhode Island: Age and Gender

	Year Licensed			
	1992	1993	1994	1995
No. males	130	190	151	180
No. females	69	69	83	84
Total	199	259	234	264
Percent females	*34.7%*	*26.6%*	*35.5%*	*31.8%*
Aver. age, males	36.5	37.3	37.6	37.6
Aver. age, females	34.2	36.3	35.1	34.5
Percent 61 or older				
males	*4.6%*	*1.6%*	*4.0%*	*3.3%*
females	*0%*	*0%*	*1.2%*	*0%*
Total No. Licensed Physicians*	2,835	2,898	3,267	3,286

*: Number of physicians with active Rhode Island licenses as per January 2 of the year signified.

Table 2

Physicians Newly Licensed in Rhode Island: Places of Birth

Place of Birth	1993	1994	1995
Connecticut	8	8	12
Massachusetts	27	23	31
Maine	2	0	0
New Hampshire	1	1	1
Rhode Island	23	17	17
Vermont	1	1	0
New England, total	*62*	*50*	*61*
	[23.9%]	*[21.4%]*	*[23.1%]*
District of Columbia	5	4	2
Maryland/Delaware	2	4	4
New Jersey	14	14	11
New York	56	45	54
Pennsylvania	12	13	10
Middle Atlantic, total	*89*	*80*	*80*
	[34.4%]	*[34.2%]*	*[30.3%]*
Southern states	16	15	13
North central states	9	22	12
Midwestern states	13	11	22
Mountain states	5	1	3
Pacific states	5	10	7
Remaining states, total	*48*	*59*	*57*
	[18.5%]	*[25.2%]*	*[21.6%]*
Canada	*4*	*2*	*6*
	[1.5%]	*0.9%]*	*[2.3%]*
Countries, other	*56*	*43*	*60*
	[21.6%]	*[18.4%]*	*[22.7%]*
Total	*259*	*234*	*264*
	[99.9%]	*[100.1%]*	*[100%]*

born physicians have consistently outnumbered those born in Rhode Island. Indeed, in 1995, close to one-third of all new licensees were born in either of these two states. The percent of newly licensed physicians born overseas has risen slightly in the last year. India, with 11 new licensees, provided more physicians to this state than any other foreign nation.

In the last decade, Rhode Island-born physicians have never numbered more than 10% of the newly licensed cadre. In the preceding decade, about 40 Rhode Islanders, each year, entered one or another US medical school.[6] An unknown number may also have attended offshore, Latin American or European schools of medicine producing an estimated 50 new physicians, identified as Rhode Islanders, annually. An average of only 19 of these have been returning each year [Table 2]. Hence, over half of Rhode Island-born physicians choose to practice elsewhere.

PLACES OF MEDICAL EDUCATION

Table 3 summarizes the geographic locations of the medical schools attended by Rhode Island's newly licensed physicians. About 85% had graduated from U.S. or Canadian schools, with about one-fourth from New England medical schools. Graduates of European schools have decreased. Not a single Italian-trained physician, for example, sought licensure in 1995 - in striking contrast to the years preceding 1992. The number of graduates of Asian medical schools, on the other hand, has increased, accounting now for 6.1% of all newly licensed physicians. Graduates of Caribbean island medical schools [other than those Puerto Rican schools fully accredited by the Liaison Committee on Medical Education] comprise 1.9% of the new licensees.

Table 4 lists those medical schools which have contributed the greatest numbers of physicians to the newly licensed groups. For the past three years Brown has provided the plurality of practitioners, displacing Tufts, which had been for years the dominant educational source for local physicians. Other important schools include the various medical campuses of the State University of New York [in Brooklyn, Syracuse, Stony Brook and Buffalo], University of Massachusetts [Worcester] and Boston University. In the years prior to 1993, Bologna had contributed material numbers of graduates to the Rhode Island's physician pool. In 1993 and 1994, however, all the ranked medical schools were in New England or the middle Atlantic states. In 1995, McGill, in Montreal, Canada, proved to be an isolated geographic exception, ranking eighth in this listing.

LICENSURE PATHWAY AND NUMBER OF ACTIVE LICENSES

Rhode Island law recognizes a number of pathways to licensure. These include certification by the National Board of Medical Examiners, state-managed FLEX examinations, the newly devised US licensure examination, Canadian province examinations or, in rare circumstances, a letter from Brown's dean of medicine stating that the candidate, possessing certain

Table 3

Physicians Newly Licensed in Rhode Island: Location of Attended Medical Schools

Medical School Region		Year of Rhode Island Licensure			
	before 1992	1992	1993	1994	1995
New England	25.6*	29.4	25.9	24.4	25.1
Mid Atlantic	29.3	26.9	31.7	33.3	29.5
USA, other	17.1	26.9	19.3	27.3	26.9
Canada	2.0	1.5	3.9	0.9	3.4
USA + Canada, total	*74.0*	*84.7*	*80.8*	*85.9*	*84.9*
Latin America**	5.4	4.5	5.0	1.7	4.2
Asia	5.8	5.0	3.9	3.0	6.1
Middle East	3.5	2.5	3.5	3.4	1.7
Africa	0.3	0.4	0.7	0.4	<0.1
Europe, west	8.9	1.5	4.2	4.7	2.2
Europe, east	2.0	1.5	1.9	0.9	<0.1
Other, total	*25.9*	*15.4*	*19.2*	*14.1*	*14.2*
Number Licensed	2,707	201	259	234	264

*: Percent
**: Includes Caribbean island medical schools.

unique investigative or therapeutic skills, is considered essential for the academic agenda of the medical school. As in prior years, National Board certification was used as the licensure pathway by about 75% of new licensees. Requests from the dean of medicine at Brown continue to provide only a negligible number of new licensees in prior years and none in 1995.

About 25% of the 264 licensees held no prior state medical licenses. Of the remainder, 34.8% held only one other active state license. About 8% had five or more licenses, and a very small number had 12 or more. Most of those with large numbers of state licenses were engaged in a *locum tenens* type of practice requiring them to move from state to state as their employing agency assigned them to a series of temporary posts. Virtually all of those engaged in such periodically mobile practices were middle-aged males. In general, the newly licensed male physicians held 1.86 out-of-state medical licenses, and the female physicians, 1.17 licenses.

SUPERVISED TRAINING

Of the 264 new licensees, 37 [14.0%] had completed two years of supervised residency training beyond their MD degree. Another 114 [43.2%] completed three years of residency training; still another 79 [29.9%] completed four years; 25 [9.5%] completed five years; and 9 [3.4%] had finished six or more years of post-graduate training [residency and fellowship.] The average number of years of graduate training for the physicians newly licensed in 1995 was 3.4 years. It is noteworthy that no American medical school graduate, in this cadre of newly licensed physicians, completed fewer than two years of graduate medical education.

SPECIALTY DISTRIBUTION

Table 5 illustrates the self-declared specialties of newly licensed physicians, by year of licensure and gender. After rising in 1994, the frequencies of those engaged in primary care [defined as family medicine, pediatrics, obstetrics/gynecology or internal medicine without any declared subspecialty] declined in 1995, both in male and female phy-

Table 4

Physicians Newly Licensed in Rhode Island: Most Commonly Attended Medical Schools*

Licensed Prior To 1993	Licensed In 1993	Licensed In 994	Licensed In 1995
Tufts	Brown	Brown	Brown
Brown	Tufts	State Univ NY**	Tufts
Boston U	State Univ NY	Tufts	State Univ NY
State Univ NY	Boston U	Boston U	U Mass
Bologna	Columbia	Columbia	Boston U
Georgetown	Pennsylvania	Dartmouth	NY Med
Harvard	New Jersey***	New Jersey	New Jersey
NY Med	Dartmouth	Cornell	McGill
Vermont	Harvard	Vermont	Yale
Jefferson	U Mass	U Mass	Columbia
Columbia	Jefferson	Geo. Washington	Einstein
Yale	NY Med	NY Med	Georgetown

*: In rank order
**: Represents medical graduates of four geographically separated campuses [Brooklyn, Syracuse, Stony Brook, Buffalo.]
***: Represents medical graduates of two geographically separated campuses [Newark and Rutgers.]

Table 5

Physicians Newly Licensed in Rhode Island: Distribution in Percent by Gender, Specialty and Year of Licensure

Specialty	Males 1993	Males 1994	Males 1995	Females 1993	Females 1994	Females 1995
Primary care*	29.5	40.4	28.3	58.0	63.9	47.6
Non-surgical specialties**	26.8	21.9	36.7	14.5	14.5	30.0
Surgical specialties***	21.6	13.2	15.6	10.1	4.8	6.0
Emergency medicine	5.3	5.3	4.4	4.4	3.6	0
Institution-based specialties+	16.8	19.2	15.0	13.0	13.3	16.5

*: Includes family medicine, general practice, pediatrics, obstetrics/gynecology and internal medicine without a defined subspecialty.

**: Includes internal medicine subspecialties, psychiatry, neurology and dermatology.

***: Includes general surgery, orthopedics, ophthalmology, otolaryngology, urology, neurosurgery and plastic surgery.

+: Includes pathology, radiology, physical medicine, anesthesiology and administrative medicine.

Table 6

Physicians Newly Licensed in Rhode Island: Sites of Birth, Medical Education, Residencies and Fellowships

Region	Place of Birth	Medical School	Residency	Fellowship
Rhode Island	6.4*	8.0	22.0	27.3
New Engl, other	16.7	17.0	22.3	23.4
USA, other	51.9	56.4	53.0	48.1
Canada	2.3	3.4	2.3	0
Nations, other	22.7	15.2	0.4	1.3

*: Expressed as percent.

sicians. The most dramatic increase has been in the declared number of nonsurgical subspecialists [e.g., cardiologists, nephrologists, etc]. The number of new general and specialty surgeons, on the other hand, has declined from 1993.

These data, of course, do not provide health care economists with convincing statistics for at least two reasons. First, a physician declaring himself a cardiologist may, in truth, be devoting two-thirds of his time to primary care. Second, newly licensed physicians constitute only about 7% of the total population of practicing physicians for that year. Therefore, their specialty distribution will not necessarily mirror the nature of practice pursued by the entire instate profession.

Who Chooses Rhode Island as a Practice Site ?

Selecting the location of one's practice is a serious undertaking. Inevitably, numerous factors motivate a physician to practice in one particular site over another - not the least of these are family obligations and commitments, the professional needs and family ties of a spouse, career opportunities in an increasingly limited job market, and such marginal elements as communities' climate and alleged cultural or recreational attractions. But to this list of variables must also be added such factors as place of birth, place of medical education, and place of residency and fellowship training. Table 6 attempts to determine which of these latter elements are statistically associated with the choice of Rhode Island as a place to establish a practice. For example, being born in Rhode Island, per se, does not seem a major factor; but if a Rhode Islander also takes his residency training in this state, the likelihood of staying instate increases at least fourfold. On the other hand, with those born beyond New England - elsewhere in the United States or even overseas - residency training or clinical fellowship in the state does not seem to be a measureable force attracting the candidate.

Board Certification

In 1994, 51.7% of new licensees had already been granted board certification in one or another defined specialty [Table 7.] In 1995 virtually the same percent [51.5%] had been apparent in the new licensees. In 1993, 9.7% of the new licensees also had board certification in a subspecialty; in 1994 this rate had risen to 15.4%; in 1995, it fell to 8.7%.

Table 7 summarizes the numbers of new licensees by specialty, gender and specialty/subspecialty certification. Since some new licensees are still undergoing residency training or have not as yet practiced sufficient numbers of years for Board eligibility, these data underrepresent the Board accreditation frequency of this cadre of physicians. In general, though, the specialized forms of surgery [eg, neurosurgery, orthopedic surgery], for reasons listed above, have lower rates of Board-accreditation among new licensees.

Observations

Certain statistical characteristics of the 1995 cadre of newly licensed physicians confirm the trends noted in the 1994 contingent of new physicians.[4] The number of newly licensed physi-

Table 7

Physicians Newly Licensed In Rhode Island: Distribution by Specialty and Board Accreditation

Specialty	Male			Female			% Boards
	No.	1^0 Boards*	2^0 Boards**	No	1^0 Boards	2^0 Boards	M + F
Int. Medicine	42	27	7	24	15	2	63.6
Family Medicine	16	8	0	9	2	0	55.6
Pediatrics	15	10	1	12	5	1	40.0
Psychiatry	26	9	3	10	7	2	44.4
Surgery, gen.	7	5	2	1	0	0	62.5
Surgery, ortho.	7	2	0	0	0	0	28.6
Surgery, other	7	3	0	1	0	0	12.5
Obstetrics/Gyn.	8	4	1	7	2	1	40.0
Ophthalmology	7	3	0	3	2	0	50.0
Neurology	7	3	0	1	0	0	37.5
Dermatology	3	3	0	2	1	0	80.0
Emergency Med.	8	5	0	0	0	0	62.5
Anesthesiology	6	3	0	2	1	0	50.0
Radiology	17	9	1	7	4	0	54.2
Pathology	4	3	1	4	2	1	62.5
Public Health	0	0	0	1	0	0	00.0
Total	180	95	16	84	41	7	51.5%

*: Board-certified in designated specialty

**: Board-certified in a subspecialty of the primary specialty Board.

cians declaring themselves as solo practitioners has dropped even further. Most physicians now entering the state for the practice of medicine do so under some sort of agreement with one of the existing acute care hospitals or under contract with an established health care organization. Only a few new licensees have joined well-established private practices in such fields as obstetrics, ophthalmology or orthopedic surgery.

Since one should distinguish between what a practitioner would like to do and what, in reality, he does, the number of Rhode Island physicians engaged in primary care remains an elusive statistic.

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The Oldest English Medical Textbook

James T. McIlwain, MD

About a thousand years ago an Englishman named Cild compiled a book of medical practice for an English physician named Bald. The book is known today as Bald's Leechbook or, as it was called in Bald's time, *Læce Boc.* A physician was called a leech (or *læce*) in those days and the remedies prescribed for various conditions and ailments were called *læcedomas* or leechdoms. Bald's Leechbook is an orderly compilation of leechdoms and it exists in a unique and beautifully written manuscript of the mid-to-late 10th century, now British Museum Royal Manuscript, 12, D.xvii. It is the oldest extant medical textbook in the English language and, for that matter, in any western language other than Greek or Latin. It would be another 3 centuries before medical texts appeared in French.[1]

The language of Bald's Leechbook is Old English or what was once called Anglo-Saxon. The latter term is now reserved by most scholars for the germanic peoples who invaded Britain in the 5th century and whose language was a member of the West Germanic branch of the great Indoeuropean language family. Old English is the language of *Beowulf* , not of Chaucer's *Canterbury Tales*, as is sometimes thought. It is in many ways as close to modern German as it is to Chaucer's Middle English, which along with its Old English forms inherited the large vocabulary descended from Latin that was introduced through Norman French after 1066. This melding of romance and germanic lexicons gives English one of the largest vocabularies of any living language.

In the transformation to Middle and Modern English, some of the Old English terms for parts of the body used in Bald's Leechbook have been retained while others have disappeared. For example we still use head (O.E. *heafod*), eye (*eage*), ear (*eare*), heart (*heorte*), liver (*lifre*), shoulder (*sculdor*), knee (*cneow*), foot (*fot*), arm (*earm*), blood (*blod*), breast (*breost*), bone (*ban*), mouth (muð), bladder (*blædre*) and navel (*nafela*). Other Old English terms have been replaced by unrelated words, as with *milte* (now spleen), *maga* (stomach), *wamb* (belly), *wange* (jaw or cheek), *heals* (neck), *l* earm (intestine or gut).[2] The family relationship of many of these terms to words in modern German will be noted by readers familiar with that language.

As is the case for virtually all medical texts of the early medieval period, regardless of their language of composition, the greater part of the material in Bald's Leechbook is derived from older sources. Scholars have devoted considerable energy to identifying these and can usually trace the material through Latin and Arabic compendia and often back to Greek texts. What is impressive about Bald's Leechbook is not the originality of its treatments and recipes, but the careful manner with which the compiler selected and organized the material from a wide range of older texts, combining it with native sources, so that the book would be useful to a physician practicing in Britain. For example, remedies based on exotic plants were largely eliminated and native words for local varieties were supplied in the recipes selected. Also the compilation is very orderly and in some ways uniquely structured. Book I of the Leechbook describes treatments for various ailments whose manifestations can be seen with the naked eye. These are introduced in the classical head-to-foot order and then followed by treatments for various skin diseases, burns, poisonings and joint pains. Book II treats disorders affecting the internal organs and unfortunately has lost a section dealing with jaundice, gynecology and disorders of the bladder and anus. This is known because the chapters are listed in the table of contents but are missing from the manuscript.

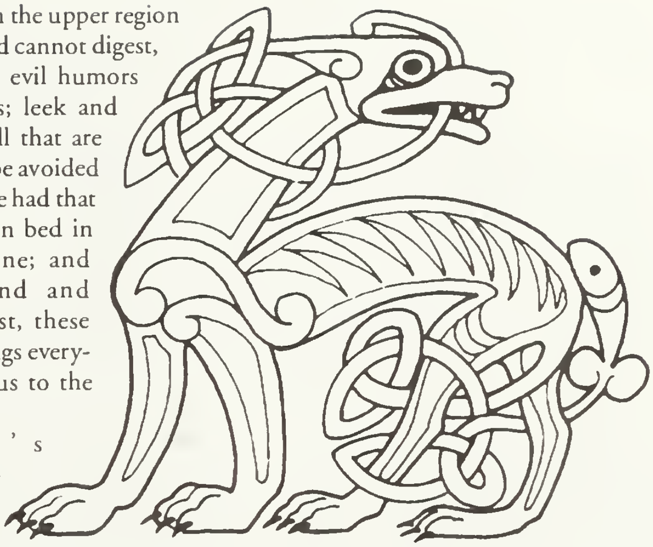
Bald's Leechbook is as innocent of modern concepts of pathophysiology as were its predecessors and as its successors would be for centuries to come. The conditions for which it prescribes are obvious blemishes (such as skin lesions, hare lip, baldness - yes, even then), fractures; assorted complaints and disabilities (such as dimness of the eyes, paralysis, inability to urinate or deliver a child), behavioral disorders; pain in various parts, animal bites, wounds and so forth. It does discuss certain conditions in detail and, from time to time, reproduces classical material related to the function of organs such as the liver or to the formation of the embryo.

The Anglo-Saxon leech recognized that diseases had to have causes but these are often identified as imbalances in the four humors or malificent agents such as worms, flying venoms or elfshot. It is interesting how many disorders are attributed to worms. There are leechdoms against tooth worms, hand worms, head worms,

small worms, dew worms, worms that vex men inwardly, flesh worms and boring worms. In most cases it is clear that the leech did not expect to see these worms, presumably because they were too small or invisible, but deduced their presence from the lesion or disorder that they caused. Although rational microbiology lay far in the future, this willingness to assign causality to unseen but physical agencies probably made the eventual leap from worms to germs not as great as one might otherwise expect. The Leechbook does not mention sin as a possible cause of disease, leaving this to the clergy.

Surgical interventions are few if one does not count the treatment of wounds, many of which must have been incurred in battle. One leechdom goes, "For hair lip, pound mastic very small, add the white of an egg, and mingle as you do vermillion; cut with a knife; sew fast with silk, then smear within and without with salve, before the silk rots. If it draws together, arrange it with the hand; anoint again soon."[3] In another we read, "If you must carve or cut off a [diseased] limb from a healthy body, then don't cut it at the boundary of the healthy flesh but rather cut or carve in that whole and living flesh so that you shall better and more readily cure it."[4]

The primary mode of treatment was medicinal and prophylactic and the greater part of the Leechbook is devoted to beverages, salves, vapors and other concoctions against the various ailments described and to admonitions about avoiding problems. A leechdom for mistiness of the eyes reveals the complexity of some of these remedies. "Take juice or blossoms of celandine, mingle with honey of bumblebees, introduce it into a brazen vessel, half warm it gently on warm coals, till it be sodden. This is a good leechdom for dimness of eyes. For the same, mingle the juice of wild rue, dewy and bruised, mingle with equally much of filtered honey, smear the eyes with that. For mistiness of eyes many men, lest their eyes should suffer the disease, look into cold water and then are able to see far; that does not harm vision, but much wine drinking and other sweetened drinks and meats, and those especially which remain in the upper region of the wamb and cannot digest, but there form evil humors and thick ones; leek and colewort and all that are so bitter are to be avoided and care must be had that a man not lie in bed in day time supine; and cold and wind and smoke and dust, these and similar things everyday are injurious to the eyes."[5]



Bald's Leechbook offers a few incantations and formulas for amulets against such things as heathen charms, fiend-sickness and certain fevers but, if their relative number is any indication, these do not seem to have played a prominent part in the practice of the professional leech. Other medical texts in Old English do speak to a thriving business in what Bald and his colleagues probably considered "alternative medicine." For example, a book called *Lacnunga* is a compendium of superstitious folk cures of ancient origin, replete with chants, charms, magic writing and grotesque concoctions. Current opinion among scholars is that there were, in fact, two classes of medical practitioners in Anglo-Saxon England. In the countryside the ill and injured probably sought out folk practitioners who applied remedies inherited largely through germanic and perhaps celtic oral traditions. Population centers supported the literate professionals who commissioned, collected and read texts like Bald's Leechbook in an effort to know and apply the most "respectable" medical learning of the past to their practices. The classical sources used in compiling this book are comparable in number and scope to anything available to continental physicians of the day. There is also evidence that leeches shared information with each other and engaged in active teaching of some kind. In Bald's Leechbook two other physicians with Anglo-Saxon names, Oxa and Dun, are credited with "teaching" certain of the remedies described. What is also clear is that leeches charged fees (*læcefeoh*), for these are mentioned, not in Bald's Leechbook, but in the Anglo-Saxon laws, a portent perhaps of things to come.

A physician was called a leech (or læce) … and the remedies prescribed for various conditions and ailments were called læcedomas or leechdoms.

It would seem appropriate to close an article about a medical textbook with a quiz. Match the Old English disorder or complaint on the left to its modern counterpart on the right. Answers in Note 6.

1. eagena sar
2. earena sar
3. eagena dymnyss
4. toð ece
5. fot adl
6. heafod ece
7. geolwe adl
8. flean
9. scorpiones stincg
10. wæter seocness
11. circle adl
12. feorthan dæges fefor
13. cneow geswell
14. healfes heafdes ece
15. stanas on blædran
16. healfdead adl

a. shingles
b. bladder stones
c. swollen knee
d. hemiplegia
e. jaundice
f. earache
g. toothache
h. eye ache
i. quartan fever
j. migraine
k. dimness of the eyes
l. fleas
m. scorpion sting
n. headache
o. foot disease
p. ascites

NOTES.

1. This article owes much to the following writings of M.L. Cameron: *Anglo-Saxon Medicine*, Cambridge University Press, Cambridge, 1993; The sources of medical knowledge in Anglo-Saxon England, *Anglo-Saxon England*, 11:135-155, 1983; Bald's Leechbook: its sources and their use in compilation. *Anglo-Saxon England*, 12: 153-182, 1984. Other important general treatments are found in Bonser, W., *The Medical Background of Anglo-Saxon England*, The Wellcome Historical Medical Library, London, 1963; Talbot, C.H., Some notes on Anglo-Saxon medicine, *Medical History* 9:156-169, 1965; Talbot C.H. *Medicine in Medieval England*, Oldbourne, London, 1967. The passages quoted here from Bald's Leechbook are slightly modernized versions of the translations in the Rev. Oswald Cockayne's edition of the Old English medical texts, *Leechdoms, Wortcunning and Starcraft of Early England*, 3 vols., Rolls Series. London, 1864-1866.
2. Old English employed several characters no longer used in Modern English. Among these the consonants eth (ð) and thorn (þ) have the value of modern 'th.' Aesc (æ) as in *læce* has no modern vowel equivalent but is believed by linguists to be similar to the 'a' in 'man', but lengthened. For purposes of the quiz note that the letter g before e at the beginning of a word is pronounced as 'y.'
3. Leechbook, I, xiii
4. Leechbook, I, xxxv
5. Leechbook, I, ii.
6. 1-h, 2-f, 3-k, 4-g, 5-o, 6-n, 7-e, 8-l, 9-m, 10-p, 11-a, 12-i, 13-c, 14-j, 15-b, 16-d.

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Health by Numbers

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by William J. Waters, Jr., PhD, and Jay S. Buechner, PhD

Births in Rhode Island, 1990–1995

Samara I. Viner-Brown, MS, and Jay S. Buechner, PhD

Since 1990, the number of births and the fertility rate among women of childbearing age have been decreasing in both the United States and Rhode Island. Both measures have fallen more rapidly in Rhode Island than nationally, and the rate of decrease in total births in Rhode Island has been magnified because the number of women of childbearing age (15 through 44 years) in the population has been declining. Within Rhode Island, especially large declines in numbers of births have been experienced among younger women (ages 15 through 29 years), among women residing in poverty areas, and among married women. Over the same period, the numbers of births among unmarried women and among women ages 30 through 44 years have increased.

METHODS

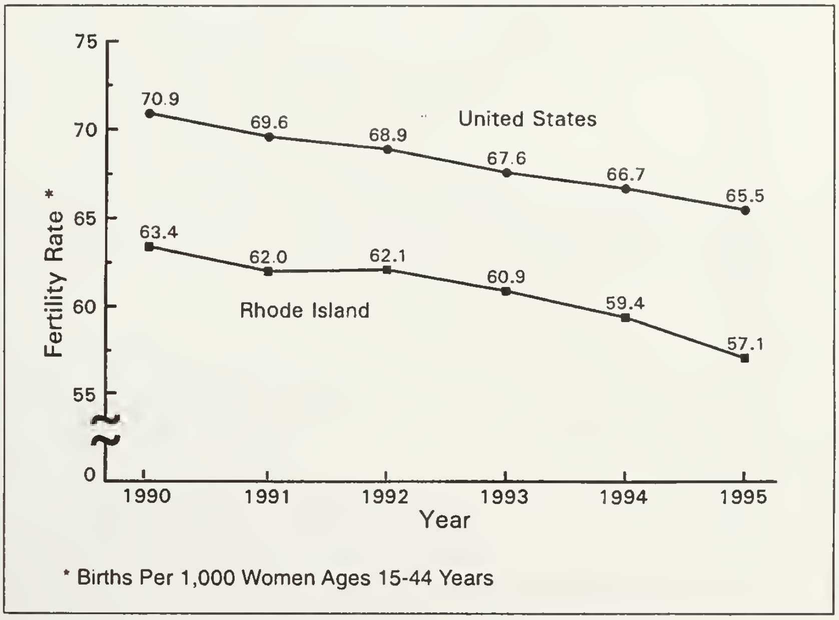
National data on births were obtained from published sources.[1,2] Data on Rhode Island births were obtained from two databases - the birth certificate database compiled by the state Office of Vital Records and data from the Universal Newborn Screening (UNS) Program, which screens every baby born in Rhode Island for developmental risk factors. Based on availability, all data presented on total births to Rhode Island resident women during the period 1990 through 1995 are from Vital Records, whereas analysis based on characteristics of the mother employed Vital Records data for the period 1990-1992 and UNS data for the period 1993-1995. Since its establishment in1993, the UNS database has shown excellent correspondence with provisional birth data compiled by Vital Records.

Neither database included births to Rhode Island resident women occurring in out-of-state facilities during the years 1994 and 1995. The numbers of such births in those years were estimated by applying a linear regression model to the numbers of such births during the years 1990 through 1993, obtained from Vital Records. For 1994, it was estimated that such births comprised 2.6% of all resident births; for 1995, the estimate was 2.4%. Where appropriate, UNS data have been adjusted by a factor reflecting the proportion of such births.

Mothers have been characterized as residing in poverty areas based on their census tracts of residence. Census tracts in Rhode Island have previously been divided into socioeconomic groups (poverty, low, middle, and high), using 1990 Census data on social, economic, and demographic characteristics[3] in a statistical methodology initially developed for use with 1980 Census data.[4]

RESULTS

Births in Rhode Island declined for the fifth consecutive year in 1995 to an estimated total of 12,722. This number is 16.2% lower than in 1990, the most recent high point, when 15,190 births were recorded. Over the same five years, births in the United



* Births Per 1,000 Women Ages 15-44 Years

Figure 1. Fertility Rate among Resident Women Ages 15-44, Rhode Island and the United States, 1900-1995.

States declined by an estimated 6.4%.

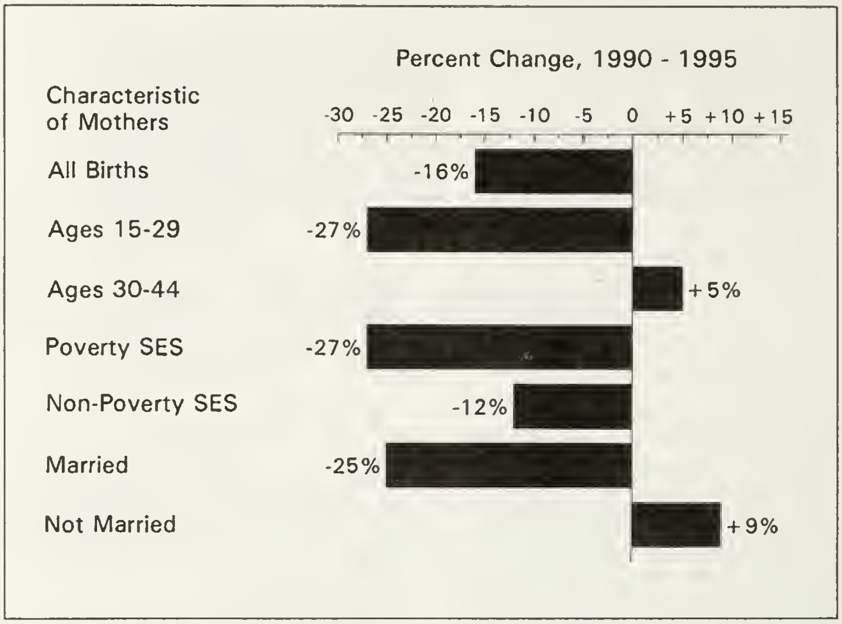


Figure 2. Percent Changes from 1990 to 1995 in Number of Births to Rhode Island Women, Total and by Selected Characteristics of Mothers.

The fertility rate, defined as the number of births per 1,000 women ages 15 through 44 years, declined by 9.9% in Rhode Island and by 7.6% in the United States from 1990 to 1995. (Figure 1) The number of births in Rhode Island declined more rapidly than the fertility rate because the estimated number of women of childbearing age in the state fell by over 7% from 1990 to 1995. In the United States, this population was increasing slowly during the period, so the number of births fell less rapidly than the fertility rate.

Within the overall decline in births and the fertility rate in Rhode Island, the experiences of different groups of women, defined by age, marital status, and socioeconomic status (SES) varied widely. Among younger women, ages 29 years and younger, the number of births fell by 27% from 1990 to 1995, whereas births among women ages 30 and older increased by 5%. (Figure 2) The large decrease among younger women occurred because the fertility rate fell by 13% (Figure 3) in a population of women ages 15 through 29 that was itself decreasing rapidly, by 16%, over the five years. In sharp contrast, among older women both the fertility rate (up 2%; Figure 3) and the underlying population (up 3%) increased slightly.

A similar dichotomy is seen in the patterns of births to married and unmarried women. From 1990 to 1995, the number of births to married women fell by nearly 25% and the number of births to unmarried women rose by 9%. (Figure 3) As a result, the proportion of births to unmarried women in Rhode Island rose from approximately one in four to more than one in three in just five years.

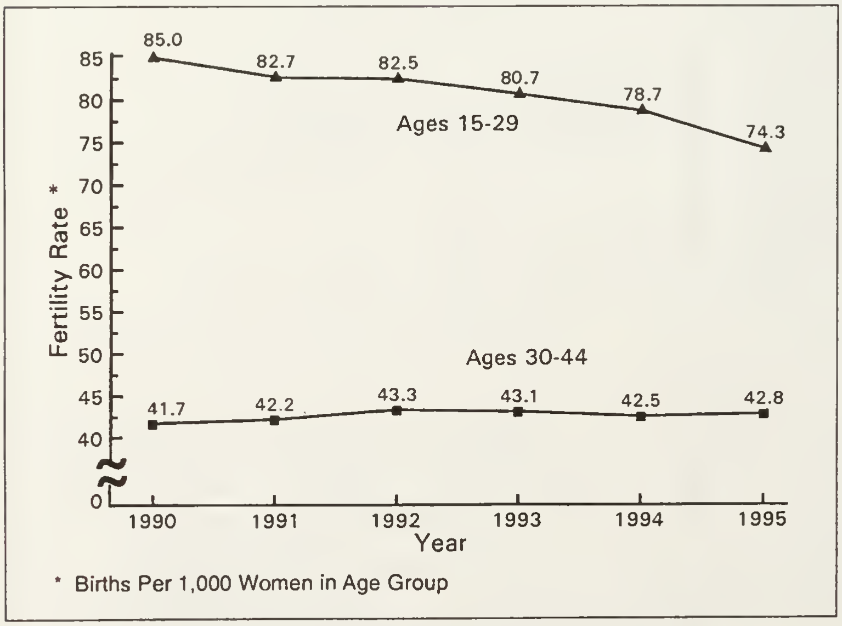


Figure 3. Fertility Rate among Resident Women Ages 15-44, by Age Group, Rhode Island, 1990-1995.

Among women living in census tracts in Rhode Island characterized as poverty areas, the decline in number of births was especially large (27%), more than twice the rate of decline among women living in other areas (12%). Within the group of women residing in poverty census tracts, the number of births fell more rapidly among women ages 29 and younger (down 31%) than among women ages 30 and older (down 11%). Similarly, the decline among married women in poverty census tracts (46%) was far greater than among unmarried women (10%).

DISCUSSION

The number of births in Rhode Island fell to a five-year low in 1995, mirroring a national trend. Besides the obvious effect on the demographic make-up of the state's population, which is already weighted heavily toward the elderly, this trend can be expected to have a substantial impact on the need for certain health care services, for day care providers, and for educational capacity in the state. It should be noted that the observed decrease in births was not accompanied by an increase in induced abortions; the number of induced abortions in Rhode Island fell by 22% from 1990 to 1994, according to provisional vital statistics.[5]

Over longer periods of time, the number of births in Rhode Island has varied as the number of women of childbearing age has changed and as their fertility patterns respond to economic, social, and medical developments. The "baby boom" of the 1950's and early 1960's was followed by a steep decline in births in the late 1960's and early 1970's, driven by the increasing availability of reliable birth control methods, severe economic disruptions emanating from local military cutbacks, and changing societal pressures. The period from 1975 through 1990 was characterized by a consistent gradual increase in the number of births, so that births in 1990 were at their highest level in two decades. The recent downturn, presumably reflecting in part the continuing uncertainty in the local economy and accelerated by the decreasing population of women of childbearing age, may signal the start of an extended period of low numbers of births annually, until a strong economic or social stimulus reverses the trend once again.

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Photographs must be in black and white, submitted on 5" x 7" glossy paper.

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Vital Statistics

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health
Edited by Roberta A. Chevoya

Rhode Island Monthly Vital Statistics Report
Provisional Occurrence Data from the Division of Vital Records

Vital Events

	Reporting Period		
	April 1996	**12 Months Ending with April 1996**	
	Number	**Number**	**Rates**
Live Births	1,259	14,203	14.3*
Deaths	790	9,557	9.6*
Infant Deaths	(10)	(96)	6.8#
Neonatal deaths	(8)	(73)	5.1#
Marriages	481	7,609	7.6*
Divorces	223	3,551	3.6*
Induced Terminations	423	5,489	386.5#
Spontaneous Fetal Deaths	88	1,099	77.4#
Under 20 weeks gestation	(87)	(1,047)	73.7#
20+ weeks gestation	(1)	(52)	3.7#

* Rates per 1,000 estimated population
# Rates per 1,000 live births

Underlying Cause of Death

	Reporting Period			
	October 1995	**12 Months Ending with October 1995**		
	Number (a)	**Number (a)**	**Rates (b)**	**YPLL (c)**
Diseases of the Heart	259	3,338	335.0	4,538.0
Malignant Neoplasms	234	2,481	249.0	6,804.0
Cerebrovascular Diseases	56	638	64.0	485.0
Injuries (Accident/Suicide/Homicide)	29	323	32.4	6,066.0
COPD	29	403	40.4	417.5

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.
(b) Rates per 100,000 current estimated population of 996,325
(c) Years of Potential Life Lost (YPLL)

Note: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

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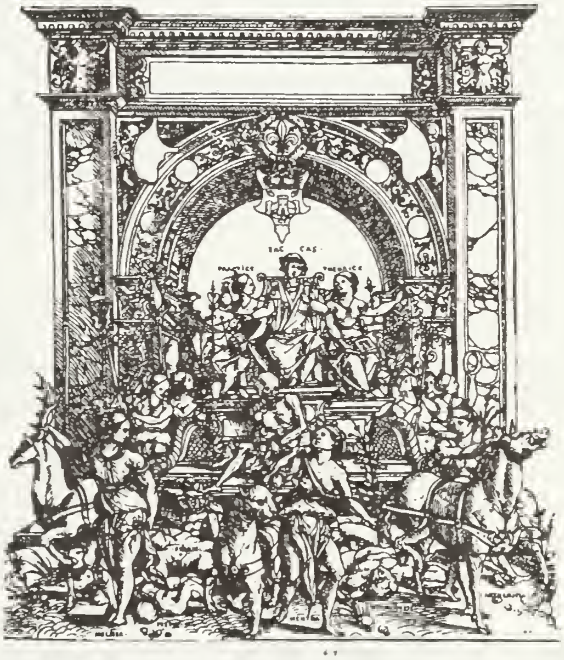
NINETY YEARS AGO

[OCTOBER, 1906]

Robert F. Noyes, MD, of Providence writes on the nature, causes and clinical identification of traumatic neurasthenia. While acknowledging that trauma per se [as in the case of the recent and tragic earthquake in San Francisco] does not always cause neurasthenia, "the fact that any became afflicted as suggested establishes the genuineness of traumatic neurasthenia." This syndrome, he notes, occurs more commonly during the active, middle years of life, and affects males twice as frequently as females. Furthermore, "religious enthusiasts, stoics, savages and people of low organization bear injuries with little suffering while the active, intelligent and highly civilized man and sensitive woman are likely to collapse under mental excitement and slight injuries."



The typical patient presents with pallor, tachycardia, irritability, depression, confusion, indecision and faulty memory. Much of the author's concerns focus on the role of the physician in the frequent instances of litigation which follow trauma.

The treatment of neurasthenia away from home is discussed in a paper by W.C. Canfield, MD, of Bristol, RI. He first summarizes the role of such physical interventions as diet, baths and exercises. Each regimen, however, must be individually designed to meet the specific needs of the patient. ["Each case of neurasthenia is a study by itself. If two cases are treated precisely alike, from beginning to end, it is probable that one of them is treated wrong."]

The home treatment of neurasthenia is discussed by Eugene Kingman, MD. Most cases, for a variety of social and economic reasons, must be cared for at home, notes the author. The therapeutic principles, therefore, rest upon providing abundant nourishment, normal incoming impulses and sufficient rest. Every neurasthenic, says the author, should have a doctor who possesses some dogmatism and the *equanimitas* recommended by Osler.

Therapy might also include the bromides, iron, quinine, arsenic and tonic doses of strichnine.

The minutes of the May 6, 1906, meeting of the Providence Medical Association are summarized. Note is made of a committee of local physicians charged with gathering donations to help in the relief work of San Francisco physicians, who are aiding victims of the great earthquake and ensuing fires.

◆

FIFTY YEARS AGO

[OCTOBER, 1946]

The lead article, written by Irving A. Beck, MD, summarizes the wartime experience of the 48th Evacuation Army Hospital, staffed by physicians largely from Rhode Island Hospital. The unit was activated in the autumn of 1942; the following spring it shipped off for the Assam province of India to provide medical coverage for the China-Burma-India theater of operations. For about two and one half years this medical unit operated in the eastern territories of India and later also in the northern regions of Burma. In late 1945, most of the unit personnel were rotated back to the States. "Drab, uncomfortable and monotonous though it often appeared at the time, now in retrospect the period in India and Burma is appreciated to have been not merely a contribution to the War effort, but a rich personal adventure."

Frank B. Cutts, MD, a senior medical officer of the 48th Evacuation Hospital, summarizes the clinical experiences of the unit while in India and Burma. During a two-year interval, about 37,500 patients were observed and treated including an awesome range of infectious diseases, many of a tropical nature, nutritional disorders such as beri-beri, and even a small number of cardiac disorders, a few of luetic origin.

J. Murray Beardsley, MD, describes the overseas experiences [surgical service] of the 48th Evacuation Hospital. The patients were variously American, Indian or Chinese military personnel and the surgical procedures were largely operative responses to battle casualties. The author provides statistics on the nature of the wounds, the operative procedures employed and the post-operative complications. A detailed discussion of retained foreign bodies within the thoracic cage concludes the paper.

Jesse P. Eddy, III, MD, discusses his experiences with sympathectomy, its history as a therapy, the anatomy of the sympathetic system, the indications for the procedure, and some statistical data on 86 such interventions.

❧

TWENTY FIVE YEARS AGO

[OCTOBER, 1971]

S.M.Aronson, MD, and H.C.Lichtman, MD, discuss the future of laboratory medicine and the role of such newer modalities as radioimmunoassay, gas-liquid chromatography, amniocentesis, and computer management of available laboratory data.

Robert S. Melville, PhD, outlines the role of automation and its impact upon the hospital-based clinical laboratory.

Applications of radioimmunoassay procedures to problems of clinical interest are summarized by Solomon A. Berson, MD, and Rosalyn S. Yalow, PhD, with particular attention to the diagnostic assay of such hormones as insulin, gastrin, and growth hormone.

Daniel P. Perl, MD, summarizes the various laboratory procedures in the prenatal diagnosis of various metabolic disorders, with particular reference to such inborn errors as Tay Sachs disease.

❧

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COMMENTARIES

Lyme Disease in Perspective

The Connecticut town of Lyme existed in a blissful state of relative anonymity for over three centuries until 1976 when a local clinician noted a clustering of patients with an atypical form of arthritis, and thus was born Lyme disease. Given a choice, it is likely that the town fathers of Lyme would have happily foregone this dubious distinction, this unwanted "limelight." Although the disease is global in distribution, the Connecticut village name for this tick-borne spirochetal disease has persisted.

Lyme, as a geographic site, is first mentioned in a 774 AD West Saxon document granting manor rights, on the southern Devonshire coast of England, to the Sherborne Abbey. Subsequent excavations of this shore site, located on the road between Southampton and the cathedral city of Exeter, indicated an even more ancient habitation, probably a Roman era village established to boil seawater, thus yielding salt. The origins of the name, Lyme, are lost to history. In Old English the word meant either a form of domesticated dog or, alternatively, it referred to the major sites of calcium oxide [limestone] deposits in the cliffs overhanging this English Channel village.

In 1284 King Edward I granted the village a royal charter, thus altering its name to Lyme Regis. As a royal borough it was allowed representation in Parliament in addition to certain mercantile privileges, particularly the importing of French wines. Lyme never possessed a really safe harbor and was periodically battered by storms from the southwest. A great seawall, called the Cobb, was eventually built to provide the port with some limited protection against the aggressive seas. This Cobb featured prominently in some of the novels of Jane Austen as well as a more recent work of fiction, *The French Lieutenant's Woman.* During the reign of Elizabeth I, a Lyme sea captain, George Somers, discovered the island of Bermuda, the basis for Shakespeare's *The Tempest.*

Lyme Regis is crammed between two physical realities: the sea on one side and great, eroding cliffs on the other. And each feature has provided the village with a small measure of fame. The seashore established Lyme as a summer resort specializing in therapeutic baths; and the cliffs yielded a wealth of prehistoric fossils securing the village as the center of English paleontological research. [It was the site where the bones of Triassic ichthyosaurs and plesiosaurs were first excavated.]

The second village of Lyme, on the eastern shore of the Connecticut River, was established in 1666 as an extension of the older township of Saybrook situated on the west shore of the river. Lyme did not appear on the Connecticut colony tax roster as a political entity, however, until 1671. It was unique amongst the early Connecticut settlements by virtue of its secular rather than ecclesiastic organization. Indeed, for some decades it had no minister of its own. In the 18th century Lyme became a center of learning, with no fewer than 38 of its citizens as graduates of Yale.

The infectious disorder, now called Lyme disease, was first recognized in Sweden, where a 1909 publication referred to it as *erythema migrans.* The first reported case in the United States, a Wisconsin patient, was published in 1969. But it was not until the seminal studies of Steere, Burgdorfer and their colleagues that its full clinical dimensions, etiology, method of spread and definitive therapy were appreciated. The intermittent symptoms included fever, headaches, stiff neck, muscle and joint pain; and in the absence of appropriate therapy, the development of chronic neuropsychiatric, cardiac and joint disease. The causative organism [the spirochete, *Borrelia burgdorferi*] was first isolated in 1982 on Shelter Island, New York. The vector of the disease is the hard-bodied deer tick *Ixodes scapularis.* There is a seasonal pattern to the acute disease with peaks in the summer months coincident with the density of the nymphal form of the tick. The animal reservoirs include deer, rabbits, mice and even birds.

Lyme disease turns out to be far less parochial than was originally presumed. And while it is now hyperendemic to the southern New England states, it has a truly worldwide distribution. After two decades of scrutiny, Lyme disease has been transformed from a curious form of arthritis to candidacy as a major emerging disease of mankind. In the minds of many, also, it has created an inappropriately high anxiety that a mere visit to New England places one at unduly high risk for the disease.

The geographic names first bestowed upon newly recognized diseases tend to prevail whether or not subsequent research shows them to be accurate. The vagaries of clinical epidemiology have thus conferred upon Lyme a tiresome burden of notoriety which is reminiscent of the grim specter borne by the equally innocent town of Huntington, Long Island. [Actually, Huntington's chorea was named in honor of Dr. George Huntington, while the town was named after one of his ancestors.] It could be worse: Beyond California, Tulare County is known solely as the source for the name, tularemia. The town of Bethlehem, sacred in Christian history, gave its name to a 16th century London asylum for the insane. People described it as a place of intolerable, unmanageable chaos and the name Bethlehem - corrupted in time to the word bedlam - became a synonym for noisy disorder. It is unlikely that the island residents of Sardinia are any more caustic than comparable populations elsewhere; nonetheless, they carry the ill-deserved stigma as the source for the word, sardonic. The Polish region of Silesia, in the 18th century, was noted for the manufacture of inexpensive cloth products. The English, acutely protective of their own developing textile industry, then took the name of Silesia as a generic description of anything which was poorly made and esthetically wanting. By the current century, the word Silesia had been modified to the word, sleazy. Obviously, it could be far worse. There was, for example, the town of Sodom.

– Stanley M. Aronson, MD

Alfred and His Excellent Medicines

The Saxon records of the centuries preceding the Norman invasion of England are scant, but one interval is better documented than others: the reign of Aelfred, king of Wessex, fourth son of Aethelwulf, and one whom current historians call Alfred the Great.

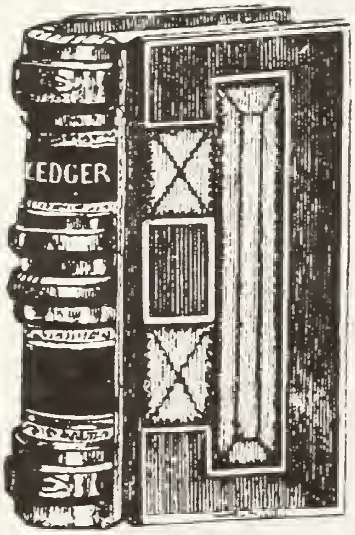
Alfred was born in the the year 848. His tutors, who schooled him in Latin and his native German, described him as a child "of singular attractiveness and promise." Twice before the age of 8 he undertook lengthy and hazardous pilgrimages to Rome. Wessex, the last of the western Saxon kingdoms, was then under virtually constant seige by the invading Danes; and Alfred's principal classrooms were therefore the battlefields of Kent and Mercia.

Alfred assumed the throne of Wessex at age 24 following the premature deaths of his father and three older brothers from some obscure, and possibly hereditary, disease. Most of his reign, some 26 years, was spent in recurrent battles with the Danes and other marauding Viking forces. Yet in all these decades of ceaseless warfare, he managed to establish a shire-based system of civil administration in southern England, a stabilized network of monasteries and a court school populated by scholars he had recruited from western Europe. Under his urging, many ancient and obscure texts were translated to the vernacular tongue. Alfred was a leader with much vision, a person of commanding and versatile intelligence, a wily soldier and yet a man of rude piety; but, say the meager archives of his day, he was also a frail human burdened by the same inborn mortal disease that afflicted and ultimately destroyed the other males of his family.

The fraternity of health care givers in ninth century England were few in number and unorganized, except for those in religious orders. Before the Norman conquest two centuries later, the number of secular physicians, then called leeches, was small. In an island beset by warfare, famine and pestilence, health care was largely rendered either by folk-healers or by monks and priests, the only literate group at that time. Therapies consisted of an intimate intermingling of syrupy electuaries, incantations, balms, astrologic advisories, salves, rudimentary herbals, purgatives, paternosters and blood-lettings. While the First Lateran Council of 1123 forbade monks from visiting the sick, the intent of this edict had been more to persuade them to adopt a more cloistered life than to prevent them from practicing medicine. Communal care continued to be an accepted moral responsibility of the Saxon clergy as well as their Anglo-Norman successors. In all of 9th century England there were but seven hospitals and no schools of medicine or recognized centers of healing. If there was any center of the healing arts, it was typically based in the larger churches and often oriented around their holy wells. [These wells, by the 14th century, evolved into the famous English wishing wells.]

Alfred maintained a continuing correspondence with many of the Church fathers. Helias, Christian Patriarch of Jerusalem, aware of Alfred's debilitating illness, sent a special messenger carrying a theriac [a molasses-based antidote designed to counteract all known poisons] and some rare and precious Holy Land medications. These pharmaceuticals included, according to the Saxon Chronicle, the following costly ointments: balsam, aloes, scammony, tragacanth and galbanum.

Balsam, sometimes called Mecca balm or balm of Gilead [Jer. 8:22], is a thick gum derived from the resinous droppings of the balsam tree and is rich in cinnamic and benzoic acids. To many it was valued more than precious metals. When the Ishmaelites bought Joseph from his jealous brothers, they paid with balm of Gilead. Balm and precious oils were also used when consecrating monarchs, thus proclaiming them rulers in the eyes of God. And when talking of Richard II, Shakespeare says: " Not all the water in the rough rude sea/ Can wash the balm from an anointed king." Balsam, a word of Arabic origin, was used in combination with other botanicals for a variety of human ailments.



Aloes, a Hebrew word, describes the dessicated juice extracted from succulent perennials of the lily family. The preparation was used principally as a purgative and, in the middle east, for embalming. It also fulfilled non-pharmaceutical, purposes: The flower of aloes, when suspended above the doorframe signified that the inhabitant was a faithful Moslem who had fulfilled his obligation of pilgrimage to Mecca. The Scriptures also mention aloes, with myrrh and cinnamon, as fragrant incenses [Psalms 45:8 and Prov. 7:17].

Tragacanth is a mucilaginous gum derived from the roots of *Astragalus,* a low growing, spiny shrub native to Persia. The name, from the Greek, means the goat's thorn, and the extracted resin may have played a role in some ancient religious ritual. It is employed, to this day, as an emulsifying or soothing agent.

Galbanum, from the Hebrew meaning something greasy, is a rank-smelling resin from umbelliferal plant roots and is said to be useful for ill-defined nervous disorders. And scammony is a strong purgative derived from the tuberous roots of *Convolvulus scammonia,* a native perennial shrub of Syria. [Rhazes, the acclaimed Persian physician, also used scammony as a contraceptive agent mixing it with mandrake, colocynth, sulfur and cabbage seed to form a pessary.]

Thus, the exotic medications which were laboriously transported across medieval Europe to aid Alfred consisted of simple purgatives, perfumes and soothing balms for nervous disorders. In a world where the heritage of Hellenic medicine had been misplaced and where any cure was regarded as a divine miracle, much naive credence was placed in empiric substances extracted from plants. It was not unusual then for these costly herbal substances - whether frankincense and myrrh or tragacanth and scammony - to be sent awesome distances as tokens of respect and reverence.

The meager Saxon records do not indicate whether King Alfred was ever treated with any or all of these herbal preparations. The records do state, however, that he died within months of their arrival.

– Stanley M. Aronson, MD

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Driving and Dementia: The Medical Perspective

Brian R. Ott, MD

BACKGROUND

Dementia is a well-recognized, age-related risk factor for hazardous driving. Editorials and review articles have addressed the issue of driving and dementia.[1-3] This article focuses on the problem of driving competence among persons with dementia in Rhode Island; its purpose is to generate local discussion and practical solutions.

The magnitude of the problem in our state is unknown. The most common cause of dementia is Alzheimer's disease (AD), accounting for 55-70% of cases, with the majority (approximately 96%) occurring in the elderly (age 65+) population. Rhode Island ranks fourth among states in the percentage of its population greater than age 64. Furthermore the prevalence of elderly residents in our state is projected to increase dramatically as the baby boom generation ages.[4]

Elderly drivers in general have an increased risk on a per-mile basis for involvement in motor vehicle accidents,[5,6] presumably due to associated medical conditions and age-related changes in cognitive, perceptual, and motor abilities. An earlier epidemiologic report in the Rhode Island Medical Journal[7] examined traffic fatalities in Rhode Island for the years 1977-1982. Although the total number of fatalities was highest among 15-24 year-old male drivers, age-related incidence rates were comparable for 75+ year-old drivers and those 15-24, with the lowest incidence for intermediate ages.

According to recent statistics from the RI Division of Motor Vehicles and the RI Government Highway Safety Office (Table 1), elderly drivers in RI contributed disproportionately to fatal motor vehicle accidents based on their percentage licensed. These figures, however, probably underestimate the relative risk of elderly drivers, since they drive 30% fewer miles compared to younger drivers.[5] Also, the degree to which elderly drivers contribute to nonfatal crashes, directly or indirectly, is unknown.

Large numbers of elderly licensed drivers in Rhode Island are probably demented or likely to become demented.

It seems likely that the rising prevalence of dementia in our elderly population could contribute more significantly to motor vehicle accidents in the future. An East Boston survey[8] found the highest estimates of dementia prevalence for a New England community: AD in 10.3% of those over 65, and 47.2% of those over 85 years. Using these statistics, the prevalence of dementia in Rhode Island may reach 19,000, an estimate comparable to the National Alzheimer's Association's 20,000.

Table I

Age Group	# Licensed	# of Fatalities	# of Drivers
0-64	559,147 (84.0%)	26 (72.2%)	29 (76.3%)
65+	106,884 (16.0%)	10 (27.8%)	9 (23.7%)

January–June 1995: Rhode Island Fatal Highway Accident Statistics

ABBREVIATIONS USED

AD	Alzheimer's disease
MMSE	Mini-Mental State Examination
UCLA	University of California, Los Angeles

Using statistics for prevalence[8] and incidence[9] from the East Boston study, the estimated number of Rhode Island elderly drivers at risk due to dementia is presented in Table 2. The incidence statistics were derived from a 4.3-year mean follow-up study evaluating 2,313 community-dwelling elders who were initially free of dementia. These figures likely overestimate the prevalence of dementia among elderly drivers, since some individuals give up their driving privileges voluntarily before their licenses expire. The prevalence figures for active driving in outpatient surveys from dementia or geriatric clinics range from 23-45%. Using this correction, the estimated number of actively-driving demented persons ranges from 2,437 to 4,768. Unfortunately, a community-based survey of dementia prevalence among the licensed elderly population has not been conducted, so these figures are rough estimations.

As to the potential administrative burden of a screening program, the incidence figures may more accurately reflect the magnitude of the task, since these figures suggest the number of elderly who may presently be "normal" but who are likely to become demented and require assessment of driving competence over time.

ARE DEMENTED DRIVERS AT GREATER RISK?

Large numbers of elderly licensed drivers in RI are probably demented or likely to become demented. Is the demented driver truly at increased risk to cause traffic accidents? While the answer generally is yes, the magnitude

Table II

Age Group	# Licensed	Prevalence (presently demented)	Prevalence (presently non-demented)	Annual Incidence (future demented)
16-64	559,147	--	--	--
65-74	68,415	2,052	66,363	523
75-84	33,733	6,308	27,425	672
85+	4,736	2,235	2,501	210
65+	106,884	10,595	96,289	1,405

Estimated number of licensed RI elderly drivers "at risk" due to dementia.

of the risk is the more important question for public safety.

One retrospective study based on review of driving records (165 dementia cases and 165 controls) found that demented drivers are approximately 2.5 times (26.1% vs 11.5%) more likely to be involved in motor vehicle crashes than age-matched non-demented drivers.[10] In this same study over 80% in the dementia group continued to drive over the three years following a crash and then had another accident in over one-third of cases. Friedland and coworkers found a 47% prevalence rate of crashes among 30 persons with AD compared to 10% of 20 age-matched controls in a retrospective survey over five years.[11] Overall there is probably a two-to-eightfold greater crash risk for elderly drivers with mild to moderate dementia compared to those not demented.[12]

How Can We Identify Those At Greatest Risk?

If one assumes that not all demented persons are incompetent drivers, then it becomes particularly important to determine the most important cognitive or functional factors that contribute to driving impairment. In a thorough examination of this issue, Drachman and collaborators[13] questioned 130 AD patient caregivers and 112 age-matched controls. The patients had an overall mean annual crash rate of 0.091, compared with 0.040 for controls.

The risk was found to rise above acceptable control rates beyond the third year of the disease. The maximum crash rate was comparable to the rate seen in 16 to 24 year-old non-demented males. Crashes per mile were not recorded, however. Therefore these figures may overestimate driving competence among demented drivers, since 65% had curtailed the number of miles they drove after the onset of illness. In this study 50% of drivers stopped driving completely by three years after disease onset. Drachman et al suggested that a three-year guideline may be helpful in defining when to be vigilant for driving incompetence among those elders with early cognitive decline.

Friedland[11] also found a rise in crashes after three years of disease. Alzheimer's disease patients who had crashes were more likely to be male; they were not more cognitively impaired on the Mini-Mental State Examination (MMSE). This study group recommended that all persons with AD be restricted from driving regardless of their dementia severity.

There has been no consistent agreement among investigators on whether general mental status screening tests or more specific tests of neuropsychological function can reliably predict driving problems. Another approach has been to use simulated or actual road tests. While this approach would seem to provide more directly relevant information, studies have generally been preliminary reports of small numbers of subjects, and have not correlated impaired test performance with driving violations or actual crashes.

Shua-Haim and Gross[14] examined predictors of performance on a driving simulation task among 41 subjects with Alzheimer's disease. A significant number of drivers who scored less than 20 on the MMSE failed the test. Activities of daily living impairment did not correlate with driving performance.

Odenheimer and coworkers[15] found that road testing of elderly and demented subjects is safe, reliable and valid. Using a 45-minute road test with both closed course and in-traffic components, 30 elderly licensed drivers with a range of cognitive abilities were examined. Performance in traffic was correlated with cognitive test scores on the MMSE, visual memory, and traffic sign recognition tests. No signifi-

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cant correlation was found with simple reaction time. Although correlation was found with the MMSE, no cutoff score discriminated those who failed from those who passed.

In a report by Hunt and coworkers,[16] 25 AD subjects with questionable to mildly severe dementia were compared to 13 age-matched controls on a one-hour road test. Forty percent of those rated as mildly demented were incompetent to drive, while those rated questionable or very mild and the normal subjects all passed the examination. General cognitive measures (Clinical Dementia Rating and the Short Blessed Test) were correlated with impaired driving performance as were more specific tests of memory, language, timed performance, visuoperceptual and attention. No correlation was found with joint mobility, strength, coordination, or primary visual abilities. Self-report was unreliable, and family assessments were equivocal in predicting performance.

A more recent road test study from UCLA examined 13 subjects with AD, 12 with vascular dementia, 15 diabetic patients, 24 normal elder and 16 younger controls. Performance in the two dementia groups was similar and differed significantly from the three control groups. Normal elders performed as well as their younger counterparts. Cognitive test scores on the MMSE, short-term memory, and visual tracking tasks correlated with driving performance. The number of collisions and moving violations per 1,000 miles were also significantly correlated with driving test performance during the two years preceding the examination.[17] This study supports the validity of road testing of demented subjects. Prospective information on crashes and traffic violations were not reported. Therefore, the predictive value of such tests is unclear. Such prospective information, though desirable, may not be obtainable from an ethical perspective, since persons clearly impaired on road tests are unlikely to be permitted to continue driving.

What Are The Present Public Policies?

In 1988 California required physicians to report dementia cases to the local health department, which forwards the information to the Department of Motor Vehicles. Physicians also must complete a four-page medical evaluation form. Persons rated as moderate to severely demented receive automatic revocation of license. Based upon the medical evaluation as well as vision, knowledge, and a 30-45 minute driving test, a decision is made to revoke, suspend, or limit driving privileges vs placement on probation or unlimited privileges. Since 1988 the frequency of patient reporting has been less than expected - perhaps due to physicians' reluctance to jeopardize the physician-patient relationship as well as to demented persons' reluctance to seek attention from physicians. To date the outcome of this mandatory reporting system has not been evaluated.[18]

The issue of medico-legal liability for physicians who do not advise demented patients to abstain from driving is not clear.

California is the only state which mandates the reporting of demented drivers. Six other states have statutes which mandate the reporting of medical conditions that impair driving. In Rhode Island reporting is not mandatory. Physicians who choose to report are protected from litigation by the reportee, and the report is considered confidential. Nine other states provide similar statutory authorization for reporting.[19] In Rhode Island drivers after age 69 must renew their licences every two years instead of every five. The renewal process involves a test of vision, but no tests of knowledge, cognitive ability, or driving competence. Concerns about physical and mental impairments may be brought to the attention of the Department of Motor Vehicles Advisory Board through multiple avenues, including self-report on the license application, observation by the licensing examiner, reports from police officers, family or physician, or a personal driving record of crashes and/or violations. This leads to a medical evaluation form, completed by the physician. A driving test may be requested. The Advisory Board relays its decision to the operator and to the Deputy Director of Motor Vehicles. Although a special restricted license is one option for the mildly impaired driver, in actual practice the driver either keeps his license with full privileges, or has it suspended.[19]

To report a demented driver, Rhode Island physicians should write to Mr. Robert Halpin, Department of Transportation, Office of Operator Control, 345 Harris Avenue, Providence, RI 02909. The letter may recommend license suspension, based on the person's medical status. If the physician is in doubt regarding the patient's driving competence, the letter may request a practical road test.

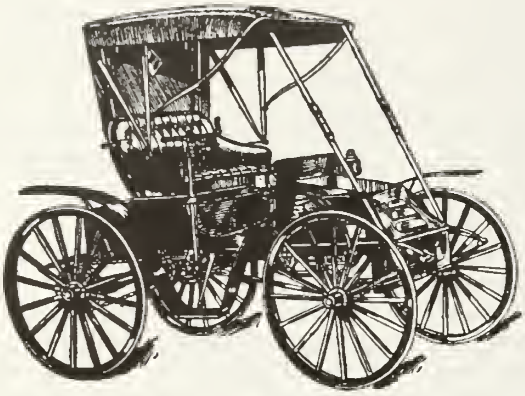
Solutions To The Problem

Unfortunately, a major crash may force the issue, compelling a demented driver to abstain. While investigators in the field agree that ultimately all demented drivers become incompetent drivers, guidelines for deciding *when* to terminate driving privileges are not well defined. Much of the research has been retrospective, based on small numbers of subjects, with differing levels of dementia severity and mixtures of dementia diagnoses, making comparisons between studies difficult.

Some investigators have suggested that all persons with a diagnosis of dementia such as AD should have their licenses revoked. Others have suggested that the decision whether or not to renew a license in an elderly driver should be based on competence rather than age *per se* or medical diagnoses.

States with required vision testing of elders have lower fatal crash rates involving elders. The addition of a knowledge or road test appears to lower the rate further.[20]

Retchin and Hillner[12] estimated the cost-benefit ratio for instituting a mass dementia screening program of all elderly drivers. Their model required all persons over age 65 scoring less than 25 on the MMSE administered by the motor vehicle registry to be referred to a physician for diagnostic evaluation. All persons diagnosed as having dementia would have their licenses revoked. This model was cost beneficial if physician evaluation fees were set at <$60.



The issue of advising a person with AD, recognized as an incompetent driver, to abstain from driving is problematic: many do not recognize their deficits - or, if they do, they minimize their significance, and do not comply. The issue of medico-legal liability for physicians who do not advise demented patients to abstain from driving is not clear. Court decisions have been divided on this issue when applied to cases of persons with other neurological disorders such as stroke and epilepsy.

The most serious threat to the elderly individual faced with the prospect of losing his driving privilege is the loss of independence. Driving may be the only way for an elder to maintain social contact or provide necessary transportation for self and spouse.[2] This quality of life factor needs to be addressed in any public policy or individual decision to revoke driving privileges. Driving restrictions should not be imposed prematurely. The reasons for termination of driving need to be discussed openly with the person, and alternative forms of transportation should be offered or provided.

Compromises such as limited driving parameters or a graduated program of driving reduction can be made, at least in the early stages of disease. "Low-risk" privileges may include short trips, slow roads, daytime driving, and non-rush hour driving. The addition of a copilot will help avoid the common crises: getting lost, running out of gasoline, or needing emergency repairs.[1]

The use of sedative medications has been reported as a risk factor for crashes among demented patients. Attention to minimizing the use of such medications and the elimination of alcohol, as well as maximizing function by treating underlying medical conditions, visual,and hearing deficits is advisable. To assist elderly drivers in evaluating and improving their skills there are several programs in the area including those sponsored by the American Association of Retired Persons, the American Automobile Association, and the National Safety Council.[19] Forced restraint from driving may be required for those dementia patients with more advanced disease who do not comply with voluntary restriction.[2] Unfortunately revocation of license does not necessarily lead to driving cessation, particularly when the patient lacks insight and judgment. As a last resort the keys can be taken away or the vehicle disabled by removing the distributor cap or the wires leading to it. The vehicle can be removed to a distant site, for "repairs." If the vehicle is sold, the money from the sale as well as the savings from insurance can pay for public transportation.

FUTURE DIRECTIONS

The burden on the physician is to determine medical competence to drive - but without clearly defined criteria for such determination. Furthermore, the physician remains in an uncomfortable ethical position: he is a patient advocate who maintains confidentiality in delivery of care, yet, for the sake of public safety, he is expected to report patients suspected to be incompetent drivers. Driving is a state-given privilege which only the state can revoke. Thus the physician has a moral, though not necessarily legal, obligation to the public at large to report.

Development of clearly defined public policy guidelines should reduce the physician's dilemma. Further research needs to define valid and reliable office screening procedures for physicians to identify those most at risk. For example, determination of cutoff scores on mental status tests or measures of instrumental activities of daily living would be useful that could predict a 95-100% likelihood that a driver would pass or fail a road test. Development of valid driving simulation tests could replace actual road testing of those identified as at risk drivers. While at the present time road testing is the "gold standard,"[3] such testing does not clearly predict performance in stress situations, and can be both time-consuming and expensive to institute on a large-scale basis.

A more widely accessible and affordable system of public transportation as an alternative to driving for the elderly also needs to be developed. This issue is being addressed by the RI Department of Elderly Affairs.

Discussions in public forums as well as among government, healthcare, insurance and automobile industries will be needed. The Rhode Island chapter of the Alzheimer's Association is addressing this issue in their public policy committee. Anyone interested in working on this committee or providing advice should contact the office at 941-522.

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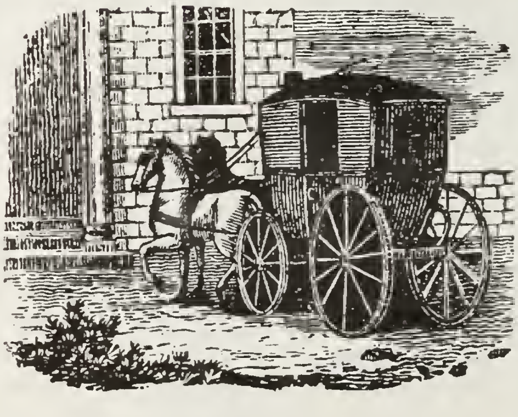

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Breast Cancer Among Asian Women

Michelle V. Nebres, ScB, and Hon Fong Louie Mark, PhD, FACMG

ABBREVIATIONS USED

BSE	Breast self examination
DHEAS	Dehydroepiandrosterone

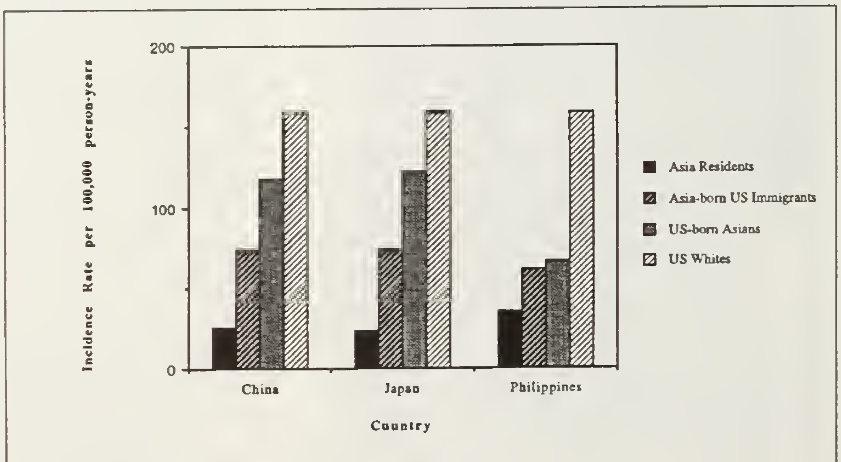
Breast cancer incidence and mortality rates among Asian women living in their countries of origin, as well as those who have migrated to the United States, are several-fold lower when compared to Caucasian women living in the U.S. This article examines various hypotheses which may account for those differences. The compilation of this information would further the understanding of breast cancer, and may contribute toward prevention and treatment, particularly among high risk populations such as United States Caucasian women. This review summarizes the differences in breast cancer incidence, genetic factors, pathologic features, and the implications for prognosis, menstrual and reproductive factors, and the environmental factor of diet among Asian and Caucasian women with breast cancer.

INCIDENCE RATES

Compared to Caucasian women, breast cancer incidence rates among Chinese- and Japanese-Americans are 50% lower for those born in their native countries, and 25% lower for those born in the U.S.[1] The incidence rates for Filipinos born either in the Philippines or in the U.S. are 40% those of Caucasians. The lowest rates of breast cancer occur in Asian women residing in Asia, intermediate rates occur in the migrating generation, and the highest rates are seen among Asians who are born in the United States. (Figure 1) Data compiled by Ziegler, et al. [2] show that breast cancer incidence rates are 60% higher among Asians born in the U.S. compared to those born in Asia. This suggests that the risk of developing breast cancer increases with successive generations of Asians living in the U.S., and points to the possibility that environmental exposures early in life influence this risk. Nevertheless, even U.S.-born Asians have at least a 20% lower rate of breast cancer compared to Caucasians, except among Japanese women under the age of fifty whose rates are similar to Caucasians.[1] This leveling may be due to the earlier migration of the Japanese to the United States. Ziegler et al.[2] showed that Asian-born women who lived in urban areas in Asia and those who lived ten years or longer in the United States are at the highest risk of developing breast cancer. In contrast, women who lived in rural areas in Asia and less than ten years in the United States have the lowest risk. Asian women with three or four American-born grandparents (particularly grandmothers) have a 50% increased risk of developing breast cancer compared to those with four Asian-born grandparents.[2] Overall, these studies show a positive correlation between the risk of developing breast cancer among Asian women and the number of years they have lived in the United States, suggesting an environmental cause for the disparity in breast cancer incidence rates.

INVOLVEMENT OF BRCA1

Genetic differences between Asian and Caucasian women may account for the variability in breast cancer seen among these two racially different populations. Currently, the predisposition to developing breast cancer has been linked to mutations involving p53, BRCA1 and BRCA2 genes. A mutation in BRCA1, localized to 17q21 (Figure 2), has been associated with early onset familial breast cancer among white women. Despite differences in the overall incidence of breast cancer in the United States and Japan, the proportion of familial breast cancer cases is approximately the same in both populations. Inoue et al. [3] found that BRCA1 mutations are not commonly associated with the development of familial breast cancer in Japan. Nevertheless, in two out of twenty families with hereditary breast or breast-ovarian cancer studied in Japan, the same mutation, resulting in a truncated BRCA1 protein, was detected in



Data compiled from Stanford, et al. 1995

Figure 1. Incidence Rates of Breast Cancer in Asian and White Women

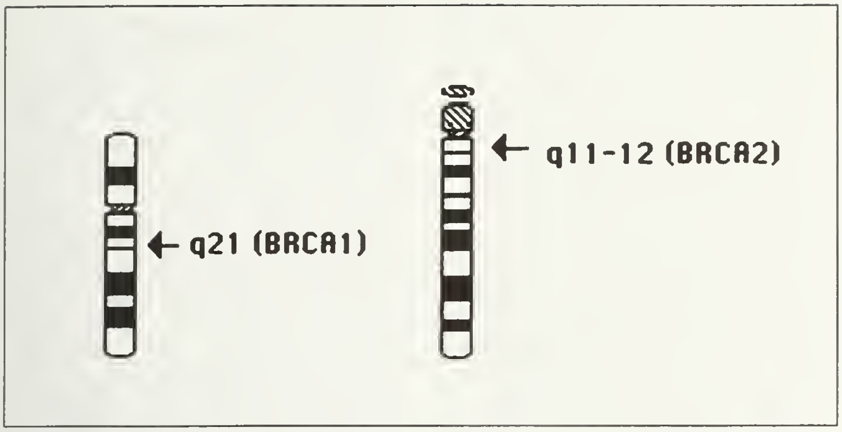


Figure 2. Ideograms indicating the locations of BRCAI at 17q21 and BRCA2 at 13q11-12.

both families.[4] It is not yet known whether BRCA2, localized to 13q11-12 (Figure 2), may be involved in familial breast cancer among Asian populations. Whether or not the same breast cancer susceptibility genes exist between Asians and Caucasians, environmental factors may influence the expression of such genes.

CLINICOPATHOLOGIC FEATURES AND IMPLICATIONS FOR PROGNOSIS

The five year survival rates among Japanese women with breast cancer were 74% versus 60% among Caucasians.[5] Sakamoto and Sugano[6] found that breast tumors among Japanese women tended to be better differentiated compared to those found in Caucasians; this may be one explanation for the comparatively better prognosis observed in Japanese women. Both Stemmermann[7] and Higuchi et al.[8] noted that histologic samples of breast cancer tumors taken from Japanese women show a higher degree of infiltrating lymphocytes, which could indicate a stronger immune response to the tumor cells. This may explain the survival advantage and decreased rate of relapse among Japanese women with localized disease. However, once Japanese women develop metastatic disease, their prognosis is usually worse than Caucasian women.[5] Relapse in the form of bone metastases is more common among Caucasians, while the common targets of metastases in Japanese women tend to be the liver and lung.[9] Higuchi et al.[8] found that race alone could predict stage as well as mortality rates among women with cancer confined to the breast, when comparing affected Japanese and Caucasian women living in Hawaii. Thus, histologic differences, the presence of metastases at diagnosis, and differences in race alone, all appear to play a role in the variable prognoses seen among Japanese women with breast cancer.

> *... these studies show a positive correlation between the risk of developing breast cancer among Asian women and the amount of time they have lived in the U.S., suggesting an environmental cause for the disparity in breast cancer incidence rates seen between Asian and white women.*

❖

DURATION OF EXPOSURE TO FEMALE SEX HORMONES

The duration of exposure to female sex hormones is a risk factor for breast cancer among women of all races. Early age of menarche, nulliparity, and first live birth after the age of thirty increase exposure to female sex hormones, particularly estrogen. Prolonged exposure to estrogen results in an increased risk of developing breast cancer because of its proliferative effect on breast tissue. Wu et al.[10] showed that menarche occurs later among Asian-born women compared to American-born Asians, which is still later than the average age of menarche among Caucasians. In addition, Asian-born women have an earlier age of first birth, more live births, and breast-feed longer then American-born Asian women. Yoo et al.[11] hypothesized that the protective effect of lactation could be due either to the suppressive effects of prolactin on estrogen secretion, or to other hormonal or mechanical effects of breast- feeding that can inhibit tumor development. One might suspect that changes in hormonal factors may account for the increased risk of breast cancer in the American-born generation of Asians. However, Wu et al. [10] found that menstrual and reproductive factors cannot fully account for the increased breast cancer incidence rates seen among American-born Asian women compared to those born in Asia. Therefore, exposure to endogenous estrogens is a common risk factor for both Asians and Caucasians, which lends support to the theory that other factors, such as environmental exposures, underly the differences in breast cancer incidence rates among Asians and white women.

DIET

The most extensively studied environmental difference between Asian and Caucasian women is diet. Yuan et al.[12] linked fiber, carotene, and vitamin C intake to a decreased risk of breast cancer among Chinese women. Since estrogens are excreted in the bile, a low-fiber diet can result in increased enterohepatic circulation, thereby exposing a woman to higher levels of endogenous estrogens and increasing her risk of breast cancer. Vitamin C and carotene have known antioxidant effects and thus may prevent tumor development.

Soy proteins found in tofu, miso, and soy milk are also hypothesized to have a protective effect against breast cancer, especially among pre-menopausal women.[13] Soy products are rich in phytoestrogens, which may act as partial estrogen receptor agonists, which block the effects of endogenous estrogens on breast tissue.[14] Makela et al.[15] hypothesized that estrogenic compounds in soy may block the *in vivo* conversion of estrogen to its active form, thereby decreasing the development of breast cancer. Administration of soy to pre-menopausal women for one month was shown to increase menstrual cycle length and inhibit the surge of luteinizing and follicle stimulating hormones.[14] This decreases a woman's exposure to the tumorigenic effects of estrogen on breast tissue, thereby lowering her risk of developing breast cancer.

While the protective effects of soy products predominate in pre-menopausal women, obesity is strongly associated with an increased risk of breast cancer among post-menopausal women. Adipose tissue provides a location for increased estrogen production. High fat diets have been associated with elevated prolactin levels, which cause the release of dehydroepiandrosterone sulfate (DHEAS), an adrenal estrogen.[16] Adams[16] found that low levels of DHEAS are seen among Japanese women, those on vegetarian diets, and fasting obese women. Thus, dietary fat, elevated prolactin levels, and subsequent production of estrogenic compounds in the adrenal gland and in adipose tissue may increase the risk of breast cancer, particularly among post-menopausal women. The American diet contains 2.7 times more fat than the Chinese diet.[17] This western diet - high in fat and low in soy products, vitamin C, and carotene - may be one of the environmental reasons for the disparity in breast cancer incidence.

Cultural Beliefs, Attitudes, and Access to Health Care

Although incidence rates for breast cancer in Asian women are lower compared to Caucasians, fewer Asian women make use of early screening procedures such as mammography and breast self examination.[18] Asian immigrants to the United States may be deterred by high costs, lack of health insurance, negative attitudes toward health care professionals, and lack of, or improper knowledge regarding, breast health. In China, unlike the United States, the majority of obstetrician/gynecologists are female. Some Chinese immigrants may be uncomfortable being examined by male physicians, because cultural beliefs dictate that male gynecologists may have contaminating effects on female reproductive processes.[19] Also, medical care in China usually involves prescribing medications at each visit. Since preventive health care measures against breast cancer do not involve medications, some Chinese women may feel that health care providers offering such services are incompetent.[19] Aside from economic and attitudinal barriers, language is another obstacle to health care for Asian immigrants. Remedies to such barriers include advertisement of free mammography clinics in Asian languages, as well as provision of female health care providers who can speak these languages. These would help inform Asian immigrants of the importance of breast cancer screening.

Breast self examination (BSE) is an effective, economical way for women to monitor breast health. BSE increases the likelihood of detecting breast cancer in its earliest stage, when treatment is most effective. Women of all races, but in particular ethnic minorities such as Asians, do not regularly practice BSE.[20] Women often give reasons such as embarrassment, fear of finding a lump, lack of skill, and belief that they are not at high risk of developing breast cancer. In order to promote this valuable technique, multilingual education concerning the importance of BSE for all women and instruction in how to properly perform BSE are indispensable. Also, health care providers must be sensitive to feelings of embarrassment and modesty due to cultural beliefs among Asian women. Thus, while Asian women may have lower breast cancer rates than Caucasian women, it is still worthwhile to provide this community with information regarding the importance of maintaining breast health in a language they can understand and from health care providers whom they trust.

Conclusion

Genetic, histologic, hormonal, and environmental factors are all important in explaining why breast cancer is not as prevalent among Asian women as Caucasian women. Since breast cancer is the most common cancer among women in the United States, continued efforts to understand the behavior of this disease, especially among low-risk populations, are important because such information has implications for the prevention and treatment of this disease in high risk groups. For instance, dietary changes that mimic an Asian diet can hypo-

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thetically decrease the risk of developing breast cancer. While details of the exact protective mechanisms governing the low breast cancer incidence rates among Asian women are now being determined, it is important to educate all women about the value of breast cancer screening. Mammography and breast self examination are currently the best ways to detect breast cancer early, when it is most treatable. Breast cancer is a ubiquitous disease affecting women of all races. Worldwide concerted efforts among the research community are necessary to further the understanding of breast cancer, in hopes of providing new strategies for disease prevention and treatment.

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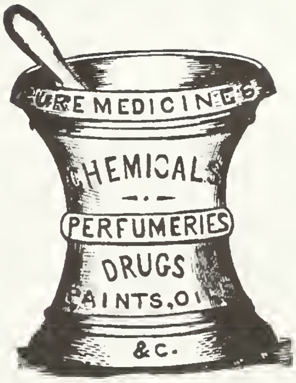

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The Clinical Spectrum of Wegener's Granulomatosis in the Elderly: Case Study and Review of the Literature

Fadi Al-Bilbeisi, MD, and Robert S. Crausman, MD

Upper and lower respiratory tract infections are common in the elderly and can usually be readily diagnosed on clinical grounds. These infections most often respond well to conservative medical treatment with antibiotics and decongestants and do not pose undue diagnostic difficulties for clinicians. There are, however, other potentially morbid, noninfectious, inflammatory sino-pulmonary disorders that need be considered in patients who present with a combination of sinus, otic and pulmonary symptoms. Wegener's Granulomatosis is one such disease entity. It is a multisystem disorder with prominent respiratory involvement that can masquerade as an infectious sinusitis, otitis or pneumonitis and is known to cause disease in the elderly.[1-3] In many, the early manifestations are mild or relapsing and can, thus, give the false impression of responsiveness to antibiotic therapy.[4] Unfortunately, if untreated, the natural history of this disorder is progressive with a very high mortality.[1,2,5] Here we present one such case and review the clinical spectrum, diagnostic approach and treatment of this disorder in the elderly.

ABBREVIATIONS USED

ANCA	Antineutrophil cytoplasmic antibody
CNS	Central nervous system
CPK	Creatine phosphokinase
CVA	Cerebrovascular accident
ENT	Ear, nose and throat
GCA	Giant cell arteritis
IV	Intravenous
NIH	National Institutes of Health
PA	Postero-lateral [x-ray view]
PAN	Polyarteritis nodosa
PMN	Polymorphonuclear leukocyte
PMR	Polymyalgia rheumatica
UCLA	University of California, Los Angeles
WBC	White blood cell
WG	Wegener's granulomatosis

Case Report:

A 77 year-old white male presented to the emergency ward with a two week history of low-grade fevers, dyspnea and a productive cough. He also noted severe, diffuse myalgias and a persistent bifrontal headache. At that time the patient reported no other complaints.

On physical examination he was an elderly male, who appeared well, alert and oriented. The temperature was 38° C; the pulse and blood pressure, normal. His room air oxygen saturation was 80%. The head and neck exam revealed prominent scalp tenderness, but was normal with intact cranial nerves, a brisk carotid upstroke without bruits and no jugular venous distention. The cardiac exam was normal, the lungs were clear and the neurologic exam nonfocal. There was no cyanosis, clubbing or edema.

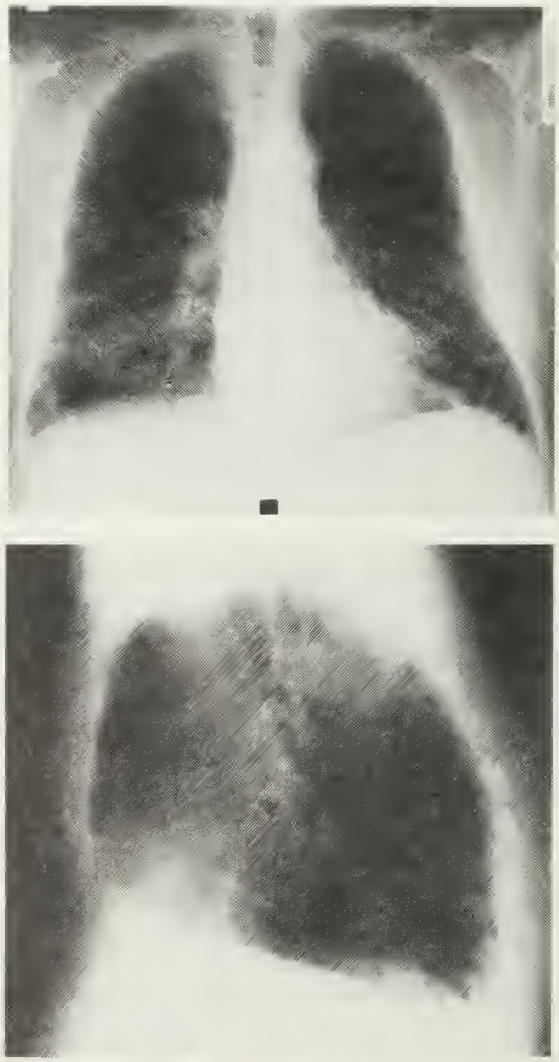

Figure 1,2 - PA and lateral chest radiographs showing a bilateral, diffuse, lower lobe predominant, nodular pulmonary infiltrate.

The admission laboratory studies showed a leukocytosis (17,500) with a prominent left shift (83% PMN's and 10% band forms), a normocytic anemia (hematocrit 33%) and normal platelets. The electrolytes, glucose, blood urea nitrogen, creatinine, CPK and liver function tests were normal. Results of a spinal tap were also normal. The erythrocyte sedimentation rate was 95 mm/hr. A temporal artery biopsy ruled out giant cell arteritis. An arterial blood gas drawn while the patient was breathing 4 liters per minute of supplemental oxygen was pH 7.46, $PaCO_2$ = 32 mmHg and PaO_2 = 73 mmHg. A sputum gram stain had many PMN's with few gram-positive cocci. The urinalysis had both white and red blood cells without bacteria or casts. PA and lateral chest radiographs

(Figure 1, 2) demonstrated a diffuse, bilateral, lower lobe predominantly nodular pulmonary infiltrate.

Wegener's granulomatosis is an uncommon, progessive, autoimmune necrotizing vasculitis with a marked morbidity and particularly high mortality in the elderly.

A community-acquired pneumonia was diagnosed and treatment with IV Ceftriaxone begun. However, the patient continued to worsen despite therapy. At this time he related a history of severe sinusitis and otitis media during the preceding year which had required tympanostomy and tubal drainage. This history of sinus and otological disease prompted consideration of pulmonary vasculitis as a possible cause of the patient's current problem. Antinuclear antibodies were positive at a titer of 1:160, C_3, C_4 and CH_{50} were normal, Rheumatoid factor was normal and Antineutrophil Cytoplasmic Antibody (ANCA) was positive; Cytoplasmic-ANCA negative and perinuclear-ANCA positive at 1:128. A thoracoscopic lung biopsy was performed; histology revealed fragmentation and destruction of the internal elastic lamina of the medium sized pulmonary arterioles (Figure 3) and pulmonary capillaritis with pulmonary hemorrhage (Figure 4), which are diagnostic of Wegener's granulomatosis. Fungal and mycobacterial stains were negative.

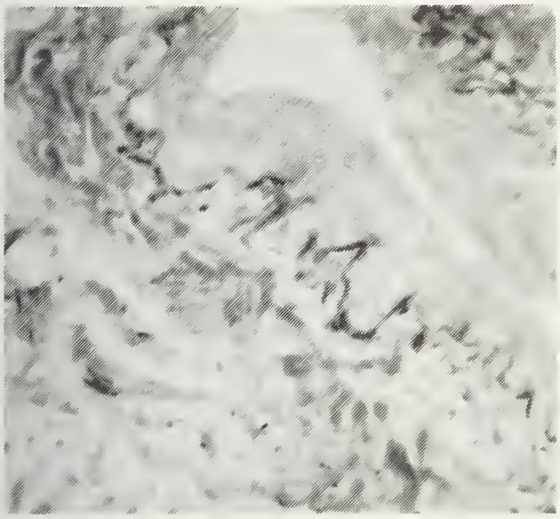

Figure 3 - Photomicrograph of lung biopsy specimen with elastin stain demonstrating fragmentation of the internal elastic lamina of a medium sized pulmonary arteriole by a necrotizing granulomatous vasculitis with multinucleate giant cells which is a diagnostic feature of Wegener's granulomatosis (magnification 250X.)

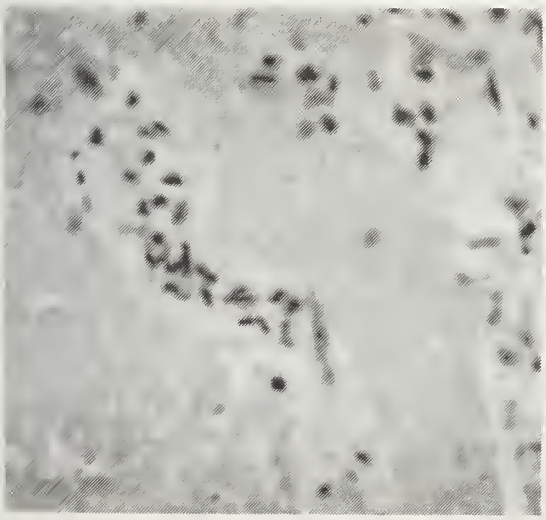

Figure 4 - Photomicrograph of lung biopsy specimen with H + E stain demonstrating a pulmonary capillaritis and alveolar hemorrhage (magnification 250X.)

Therapy with high dose intravenous steroids (125 mg methylprednisolone q 8 hours) and oral cyclophosphamide (2 mg/kg) was instituted; and the patient was markedly improved within 24 hours, with complete resolution of his pulmonary infiltrates and headache by 72 hours. He has since been in complete remission for over two years and has been tapered off of all steroids and continues on low dose cyclophosphamide (25 mg/day).

DISCUSSION

Wegener's granulomatosis (WG) is an autoimmune necrotizing vasculitis that is often classified as a pulmonary-renal syndrome because of the very high frequency of respiratory and urinary tract involvement.[1,5,6] It is clear, however, that WG is not limited to the respiratory and urinary tracts, but is truly a multisystem disorder that can occur in all age groups. The peak incidence is in the 5th decade of life, but cases have been described in the elderly.[1,2,7] The systemic nature of this illness is underscored by the National Institutes of Health (NIH) experience where 158 patients have been followed for between 6 months and 24 years.[1] In this series fever was often present (50%) and many (67%) had musculoskeletal involvement with arthralgias, myalgias, myositis and even inflammatory monoarticular, pauciarticular or migratory arthritis at some point in their course. Similarly, neurologic manifestations with mononeuritis multiplex (15%) and/or CNS involvement (8%; CVA, cranial nerve palsy or diabetes insipidus) were frequent. Associated temporal arteritis has been described, and as in this case, the disease can mimic features of polymyalgia rheumatica (PMR)[9] or giant cell arteritis (GCA).[10,11] Cutaneous findings of palpable purpura, vesicles or subcutaneous nodules (46%) were common in the NIH series. Pericarditis occurred in 6% and conduction system disease has been reported elsewhere.[12] Ocular manifestations (15%) in this series were mild, although sight-threatening uveitis, optic neuritis and retro-orbital pseudotumors have been reported elsewhere.[13] Renal involvement with glomerulonephritis was present in 20% at diagnosis and occurred in 77% overall. Pulmonary symptoms were ubiquitous and prompted the diagnosis in 90%. ENT abnormalities were present in 73% at diagnosis and 92% overall (serous or purulent otitis media in 25%).

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has looked specifically at Wegener's granulomatosis in a geriatric population[2] stratified 46 patients from the University of California Medical Center affiliated hospitals into two groups: subjects over the age of 60 (n = 12) and under 60 (n = 34). The clinical spectrum of disease presentation in terms of organ system involvement was indistinguishable between the two groups. There was, however, a significant delay in diagnosis in the older versus the younger group (mean 7 vs. 2 months). Further, there was a marked hesitancy of clinicians to institute aggressive therapy for the older group, with only 58% receiving cytotoxic treatment at diagnosis compared with 82% of the younger group. Not surprisingly, there was a profound difference in mortality with the older group doing much worse over 2 years (86% vs. 10%).

DIAGNOSIS OF WEGENER'S GRANULOMATOSIS

Diagnosis of this disorder first requires a high level of clinical suspicion. Given its protean manifestations and often indolent nature early in its course it should be a consideration in the differential diagnosis of any patient who presents with new onset sino-pulmonary infections, otic complaints, hematuria or poorly explained rheumatic or constitutional complaints.[2] It is possible that in the UCLA series[2] the large difference in mortality between the older and younger patients may, in part, have been due to the general delay in diagnosis. Thus, it is important that Wegener's granulomatosis be an active diagnostic consideration in the appropriate setting.

The serologic evaluation can be of value and will often secure the diagnosis. The nonspecific findings of an elevated erythrocyte sedimentation rate, positive anti-nuclear antibody titers, a positive rheumatoid factor or circulating immune complexes are interesting, but rarely helpful. Immunoglobulins G, A or E can also be nonspecifically elevated.[14,15] Complement (C_3, C_4, C_{50}) levels are usually normal.[8] In contrast, the antineutrophil cytoplasmic antibody (ANCA) is a very useful serologic test. There are two patterns of ANCA; the cytoplasmic or C-ANCA and the perinuclear or P-ANCA. The C-ANCA is thought to be specific for Wegener's granulomatosis, but has only a 75% sensitivity. The P-ANCA is a much more sensitive test for systemic vasculitis than is the C-ANCA, but can also be positive with microscopic polyarteritis nodosa (PAN), Churg-Strauss or overlap syndromes. The ANCA likely have an etiologic role in the pathology of these disorders and, thus, their description is of more then diagnostic interest and may even be used to gauge the effectiveness of therapy.[8,16] Unfortunately, many laboratories do not routinely perform ANCA testing; consequently, it may be several days before results are available.

Tissue diagnosis remains the standard of care in most cases, particularly if their course is rapidly progressive. Cutaneous and upper airway biopsies are generally nonspecific, but can occasionally be helpful. Temporal artery biopsies have on occasion been reported to be diagnostic,[10,11] but as in this case, most often are normal even when headache is a prominent feature. Renal biopsy most often demonstrates a focal-segmental necrotizing glomerulonephritis which can be rapidly progressive with scant immune complex deposition[1] and is sufficient to confirm the diagnosis in many cases. Medium-sized vessels, however, are not obtained with a routine needle biopsy of the kidney and, thus, lung biopsies are preferred with a yield approaching 100% when there is respiratory tract involvement.[1,8]

TREATMENT OF WEGENER'S GRANULOMATOSIS

Wegener's granulomatosis, which had been historically uniformly fatal, has proven to be remarkably responsive to cytotoxic therapy. It is now possible to induce a remission in 75 - 90% with a 5-year survival approaching 80%. The elderly do tolerate cytotoxic treatment for WG and do respond similarly to younger patients given similar duration and severity of symptoms.[2] Many have lasting remissions and can be tapered off therapy.[1,2,8] Current recommendations, based upon the NIH experience, are (1) daily oral therapy with prednisone 1 mg/kg body weight and cyclophosphamide 2 mg/kg with subsequent dosing adjusted to maintain a WBC count of ≥ 3,000 - 3,500, or in rapidly progressive cases (2) prednisone 2 - 15 mg/kg and cyclophosphamide 3 - 5 mg/kg. Steroid therapy is usually continued for the first one to two months and then tapered to alternate day therapy. Cyclophosphamide is generally continued for one year and then tapered by 25 mg per month. Alternately, there is ongoing investigation into the use of monthly intravenous "pulse" cyclophosphamide therapy at 500 - 1,000 mg/M^2 body surface area.[17] Azothioprene has been suggested as an alternative cytotoxic agent to patients intolerant to cyclophosphamide, but experience is limited.[8] Similarly, trimethoprim-sulfamethoxazole (Bactrim) may have a therapeutic role beyond prophylaxis against *Pneumocystis carinii* superinfection in those on cytotoxic agents, but this remains to be defined.[18]

CONCLUSION

Wegener's granulomatosis is an uncommon, progressive, autoimmune necrotizing vasculitis with a marked morbidity and particularly high mortality in the elderly. Further, it most often affects older adults and as many as 25% of cases occur in the elderly.[2] There is usually multisystem involvement and it can mimic many different disease conditions.

Diagnosis can be suspected on clinical grounds and confirmed by either serologic testing for antineutrophilic cytoplasmic antibodies or by tissue biopsy. Treatment with immunosuppressive and cytotoxic agents is effective in the elderly and should be instituted early in the course of the disease.

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A Woman With a Balanced Autosomal Translocation Who Received Chemotherapy While Pregnant

William Y. Kim, BA, Tarek W. Wehbe, MD, and Wallace Akerley III, MD

Cancer is the second leading cause of death in women during the reproductive years, with malignancy complicating the course of approximately 1 in 1000 pregnancies. A significant number of these neoplasms require treatment with chemotherapeutic agents forcing the physician to balance the possible damages to the fetus against the adverse effects to the mother resulting from delay of treatment. Antineoplastic agents disproportionately exert their effects on rapidly proliferating cell populations. Fetal tissues, by virtue of their high growth rate, are especially susceptible to the damaging effects of chemotherapy, particularly throughout the first trimester, a critical time for the central nervous system and vital organs. This hypothesis has been confirmed in animal models; extrapolation to humans, however, remains in the realm of theory.

We present here a case report of a young woman with a balanced autosomal translocation who received two cycles of cyclophosphamide, adriamycin, and cisplatinum (CAP) during the first trimester of pregnancy for adenoid cystic carcinoma of the submandibular gland. Her premature infant was born with blepharophimosis, microcephaly, hydrocephalus, and the same balanced translocation.

CASE REPORT

The patient is a 29 year-old Hispanic female with a past medical history of adenoid cystic carcinoma of the submandibular gland which was treated with surgical excision and radiation therapy in Puerto Rico four years prior to presentation. She was admitted to Rhode Island Hospital for shortness of breath and wheezing. Work-up included a chest radiograph, which revealed multiple, 1-2 cm soft tissue densities throughout both lung fields. She had a negative mammogram; an ultrasound and CT scan of the pelvis showed minimal enlargement of the uterus but no evidence of an intrauterine pregnancy.

ABBREVIATIONS USED

CAP	Cyclophosphamide, adriamycin and cisplatin
CNS	Central nervous system

Fetal tissues, by virtue of their high growth rate, are especially susceptible to the damaging effects of chemotherapy, particularly through the first trimester.

CT scan of the chest revealed multiple pulmonary nodules with no lymphadenopathy. Alpha-fetoprotein and beta-human chorionic gonadotropin levels were within normal limits. On hospital day 8, a CT guided needle biopsy of a peripheral lung nodule was performed, the pathologic study of which showed adenoid cystic carcinoma consistent with a recurrent submandibular gland tumor. The patient was subsequently found to have elevated beta-human chorionic gonadotropin levels. An intrauterine pregnancy was confirmed by ultrasound.

After extensive discussion with the patient about the poor prognosis and lack of effective therapy, it was agreed to try a chemotherapy combination based on a published study which reported a response rate of 36% in patients treated with the monthly combination chemotherapy of CAP.[1] A therapeutic abortion was scheduled the following week. The chemotherapy regimen consisted of cyclophosphamide (500 mg/m^2), adriamycin (50 mg/m^2), and cisplatinum (100 mg/m^2) given every month. She received 2 cycles, coinciding with 5 weeks and 10 weeks of gestation. With chemotherapy, the patient's dyspnea dissipated and at approximately 14 weeks of gestation she decided that she would like to keep the child despite our concerns and explanations as to the possible teratogenic effects the chemotherapy might exert on the fetus. No further chemotherapy was given after this point.

At approximately 25 weeks of gestation she presented to the hospital as a gravida 7, para 5 with the complaint of sudden bleeding and passing of clots per vagina. Real time ultrasound revealed a frank breech presentation with an estimated fetal weight of 912 gm. Magnesium sulfate was used to slow labor; however, the patient continued to progress through labor and the baby was delivered by emergency cesarean section.

Apgar scores were 1 and 6 at 1 and 5 minutes respectively. The baby was intubated at 55 seconds of life because of respiratory distress and transferred to the neonatal intensive care unit. On exam, the baby showed a Dubowitz score of 27 weeks; its length was 36.5 cm (70%), weight 1020 gm (70%), and head circumference 23.5 cm (30%). Head, eyes, ears, and nose exam revealed a slightly elongated anterior-posterior diameter, high forehead, narrowed biparietal diameter of the skull, and anterior and posterior fontanelles both open and flat. Examination of the eyes revealed fused and small palpebral fissures (blepharophimosis) measuring 1 cm in diameter. The ears were normally set while the nose appeared bullous with a prominent nasal bridge, and patent nares. The back was straight and without dimples or tufts. Genital exam revealed bilateral enlarged testes with the left testis within the inguinal canal. On neurological exam the child moved all four extremities, showed no evidence of seizures or jitteriness, and had normal primitive reflexes.

On hospital day 1 a cranial ultrasound was obtained for routine evaluation of possible intraventricular hemorrhage. It revealed moderately to markedly symmetrically dilated lateral ventricles; the margins were irregular, having a nodular appearance suggesting the possibility of cortical hypertrophy; the corpus callosum was attenuated; and within the tectum, at the level of the aqueduct of Sylvium, were symmetric small echogenic foci of uncertain etiology.

Echocardiogram obatined on hospital day 3 showed an atrial left-to-right shunt consistent with a patent foramen ovale. Repeat cranial ultrasound on hospital day 11 and 30 showed no further change.

Finally, cytogenetic studies showed both the baby and mother to have balanced (9,16) translocations.

DISCUSSION

Antineoplastic agents, by inhibiting cell replication, exert their maximum deleterious effects on rapidly dividing cells such as the bone marrow, intestinal epithelium, gonads, and hair. Since a rapid rate of cell division characterizes the fetal state, it is predictable that the fetus will be especially sensitive to the effects of anticancer agents.[2] Indeed, the data illustrate that anticancer drugs are teratogenic and mutagenic in a variety of laboratory animals.[3] In some cases, the teratogenic dose borders on the maximal antitumor dose; however, in many other instances the therapeutic window is such that no ill effects are seen until the therapeutic dose is well exceeded.[4]

Specific malformation can be reproduced in animals based on the specific agent, dose, and time of administration. After giving cyclophosphamide to pregnant mice, Gibson and Becker observed a variety of predictable manifestations in their offspring, including exencephaly, cleft palate, and multiple skeletal defects (adactyly, syndactyly, and missing ribs).[5] With humans, however, the frequency and types of malformations are much less predictable.[3] Finkbeiner reports that the fetus may be affected systemically by such drugs, including effects such as hematopoietic depression, infection, secondary to leukopenia, and hemorrhagic phenomena.[6] A clear-cut extrapolation from animals to humans appears tenuous, with most data indicating less danger than that anticipated from theoretical considerations or data derived from experiments in laboratory animals.[2,4,7]

The danger to the fetus appears to be influenced primarily by the dosage of the drug and gestational age of the fetus.[2,4] Sokal and Lesserman, reviewing 50 reports of pregnant women who received chemotherapy at any time during their pregnancy, found 8 instances of fetal abnormality (16%), 16 spontaneous abortions (32%), and 7 therapeutic abortions.

No obvious fetal malformations were observed in infants born to mothers who received chemotherapy after the first trimester of pregnancy.[2] Nicholson reviewed a series of 185 reports of pregnant women who received chemotherapy prior to 1967: 110 were given chemotherapy during the first trimester. In 68 cases the status of the child was recorded; 15 children had fetal abnormalities (22%). Ten of these malformations occurred after administration of aminopterin, the other five after giving mercaptopurine, chlorambucil, cyclophosphamide, and busulphan. Malformations were not specified. Seventy-five women received chemotherapy in the second and third trimester; in 73 cases the record of the infants was available, showing no malformations.[8] These data are consistent with two more recent reviews by Schapira and Chudley (1984) and Doll et al. (1989), who reported malformation rates of 12.7% and 17% respectively in pregnant women who were given chemotherapy in the first trimester.[9,10]

Although both serious congenital anomalies and spontaneous abortions occurred in patients receiving chemotherapy in the first trimester, it should be remembered that these complications while not inevitable are nonetheless five-fold greater than in the offspring of noncancerous patients.[6,9] The first trimester of pregnancy, during which organogenesis occurs, is undoubtably the period in which the fetus is most vulnerable to anitcancer agents. In contrast, neuronal growth in the brain continues throughout this time, but in general, no adverse effects to administering chemotherapy have been reported. Most investigators concur that the risk of fetal malformation following chemotherapy in the second and third trimester is minimal.[4,7,11]

Although combination chemotherapy would seem to be more detrimental than single-agent chemotherapy, Doll et all showed in a series of 45 patients that exposure to a combination of agents did not increase the frequency of malformations over that of single-agent chemotherapy. Seven of 45 fetuses were affected (16%), a rate similar to that quoted for single-agent chemotherapy.[9] Blatt et al, however, state that while single agents may be used alone with relative safety, the same agents used in combination may be teratogenic. For example, in Sokal's review of patients, busulphan and 6-mercaptopurine were given alone without causing malformations. When given together, they were associated with congenital anomalies including micropthalmus, corneal opacities, cleft palate, and hypoplasia of the thyroid and ovaries.[2,11]

The fetus was exposed to the ionizing radiation of CT scan. Studies on animals, follow-up of Nagasaki and Hiroshima victims, and accidental exposure of fetuses in suspected pregnancies - all demonstrate that ionizing radiation may be injurious to the fetus. Common fetal effects of radiation exposure include growth retardation, cataracts, malformations including microcephaly and associated CNS conditions, and death. These radiation effects, much like chemotherapy, are related to dose, dose rate, and gestational age.[12] The fetus' gestation is typically divided into three stages based upon radiational effects on its outcome. The first stage, preimplantation and early implantation, occurs between days 0 and 10 of gestation; (radiation produces an all-or-none efffect, either destroying the embryo or having no effect). The second stage, organ system formation, occurs between days 11 and 56 of gestation with radiation exposure causing visceral organ or somatic damage. By the third stage, after day 56, organogenesis is complete and larger doses of radiation are required to produce malformation. In this state, however, the nervous system is still developing and remains vulnerable.[4]

Dekaban in 1968 described 26 fetally irradiated patients. He showed that modest doses (around 250 rads) given before 2 to 3 weeks of gestation may increase the spontaneous abortion rate but was not likely to induce severe congenital anomalies. A similar dose given between 3 to 20 weeks produced anomalies in over 50% while in cases over 20 weeks no severe anomalies were observed.[13]

Diagnostic radiation exposure may be safe; however, long-term studies are not conclusive and some congenital anomalies after diagnostic procedures performed during the first trimester have been reported.[5,12] Most authorities recommend therapeutic abortion if radiation expsoure exceeds 10 rads.[14]

In regard to the specific agents administered during this pregnancy, alkylating agents especially cyclophosphamide when given during the first trimester, have been asociated with major and minor malformations including absent toes, single coronary artieries, and umbilical and inguinal hernias.[11] No abnormalities have been reported with adriamycin during various gestational ages.[15] In fact, one investigator, by showing the absence of doxarubicin in the amniotic fluid of a patient 4 and 16 hours after its administration, suggested that the placenta may offer some protective effect to the fetus.[4]

Our patient's child was born with blepharophimosis, hydrocephalus, and microcephaly after the administration *in utero* of CAP at 5 and 10 weeks gestation. Given the review of the literature above, the combination chemotherapy is the most likely basis for these congenital anomalies. However, both the fetal irradiation by pelvic computed tomography at 5 days gestation and the inherited balanced (9,16) chromosomal translocation which might have become unbalanced may be partially or wholly responsible.

Chemotherapy during the first trimester has consistently beeen reported as causing congenital anomalies at rates of 12-22%.[1,8,9] In addition, the timing of administration, at 5 and 10 weeks gestation, coincides with the highly sensitive periods of development for the eyes, CNS, heart, ears, limbs, and external genitalia. However, the fetus in our case was exposed at approximately 5 days gestation, placing it in the preimplantation and implantation stage. According to Dekaban, the radiation should have caused an all-or-none effect, increasing the spontaneous abortion rate but not inducing congenital anomalies.[13]

Both the mother and child in this case had a (9,16) balanced translocation. Wenger et al[16] suggested that offspring of normal individuals with an apparently "balanced" karyotype might be at greater risk for significant birth defects. Looking at a series of six families where both a parent of the proband and the proband had the same balanced reciprocal automal translocation, the authors found that fragile sites were associated with 83% of the translocation breakpoints, greater than that by chance ($p<0.025$). They proposed that these fragile sites are unstable areas predisposed to breaks and unequal crossing-over during meiosis, creating minor duplications and deletions. Therefore, neonates inheriting a seemingly "balanced" karyotype from a normal parent with a balanced translocation may be at increased risk of being malformed (micrognathia, tracheoseophagel atresia, skeletal abnormalities, microcephaly, and macrocephaly) or developmentally delayed because of submicroscopic chromosomal malformations.

We postulate that the child's congenital anomalies are most likely due either to the combination of chemotherapy, the inherited balanced translocation, or both. Although the pelvic CT scan most likely did not contribute to the child's malformations, it has been shown that *in utero* exposure to diagnostic x-rays leads to an increased incidence of childhood cancer (approximately 40%), including acute leukemias and CNS neoplasms.[5] Therefore, long-term follow-up of this child is warranted.

The use of chemotherapy in pregnancy evokes moral and philosophical questions, as well as complex medical decisions. The importance of long-term studies of fetuses exposed to chemotherapy is highlighted by the observation that rats, normal at birth, and exposed to busulphan *in utero*, manifested later sex hormone deficiencies and sterility.[11] Report of adenocarcinoma of the vagina in young women exposed to diethyl stilbesterol *in utero* also underscores the necessity for long-term follow-up of patients exposed to chemotherapy *in utero*. To our knowledge no long-term observations have chronicled the possible sequelae of fetal exposure to chemotherapy (e.g., impairments in growth, development, learning, reproductive function, or carcinogenesis).

The survival rates of cancer patients continue to improve - confronting obstetricians with the challenges of managing and counseling the pregnant patient with a malignancy. The severity of the malformation and side-effects mentioned above would seem to rule out the use of chemotherapy during pregnancy. However, both the mother and fetus are at risk - the mother from cancer, the fetus from treatment. Delaying or compromising treatment on behalf of the fetus may jeopardize the health and life of the mother. Yet Schapira eloquently states that these fetal malformations are not inevitable.[10]

Lastly, our case teaches that underlying genetic defects may be responsible for congenital malformations which appear to have an obvious explanation. The birth defects described could easily be attributed to the damaging effects of chemotherapy administered while the child was *in utero.* But cytogenetic studies revealed the inherited balanced translocation. We can only wonder whether the past reports of malformations attributed to chemotherapy or radiation might have had an underlying genetic cause.

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Kinesthesia

Michelangelo claimed his David resident
of a marble block the sculptor chipped, hesitant

as he unsealed stone from the young man's skin.
David cannot give his thoughts of being held in:

if he enjoyed his time within the rock, not once
averse to missing his Renaissance;

or if he loathed for ages the marble womb
which held him until chiseled and exhumed.

Michelangelo never claimed he heard David ask out,
but now ladies come and go about

the room where David stands, high in the air
above crowds which saunter to see him bare.

Kinesthetically, his situation has not improved
for, while no longer enmarbled, he cannot move.

He will not go soft, his eyes cast in persistence
toward walls defining his latest existence.

Ron Willy

Ron Willy, BA, is a medical student at Brown University ('99). He completed his undergraduate studies at Marquette University and his post-baccalaureate pre-medical studies at Bryn Mawr College.

Health by Numbers

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by William J. Waters, Jr., PhD, and Jay S. Buechner, PhD

Melanoma of the Skin in Rhode Island

John P. Fulton, PhD

Malignant melanoma of the skin will claim an estimated 7300 lives in the United States in 1996.[1] In Rhode Island, an average of 27 residents died of the disease annually during the period 1990-1994. As in the U.S., melanoma victims in Rhode Island are predominantly white (100 percent during the years 1990-1994), and male (57 percent during the years 1990-1994).

Melanoma mortality has increased steadily in the U.S. since the 1950's (Figure 1).[2,3] During that decade, the annual melanoma death rate, age-standardized using the 1970 U.S. population,[2] was about 1.0 per 100,000 among white females and about 1.3 per 100,000 among white males. By the early 1990's, the melanoma death rate had almost tripled among white males (3.5 per 100,000 in 1990-1992), and had nearly doubled among white females (1.7 per 100,000 in 1990-1992).

Melanoma mortality rates in Rhode Island have mirrored the national experience except in the 1980's, when the age-standardized mortality rate in Rhode Island for white males (5.3 per 100,000) far exceeded the comparable U.S. rate (3.1 per 100,000).[2] Fortunately, this differential has not been sustained, and the current age-standardized Rhode Island rate for white males (2.9 per 100,000 in 1990-1994) is lower than the current U.S. rate (3.5 per 100,000 in 1990-1992). The melanoma mortality rate is subject to wider variation in Rhode Island than the U.S. because the former is based on far fewer annual deaths (currently about 27) than the latter (currently about 7300).

Cancer incidence data, including melanoma, have been collected since 1973 by the Surveillance, Epidemiology, and End Results (SEER) system of the National Cancer Institute, which covers about one-tenth of the U.S. population. The SEER system uses substantial resources to assure that its incidence data are complete, reliable, and nationally representative. Melanoma incidence statistics from the SEER system are considered to be of the highest quality obtainable.

Statewide melanoma incidence data have been collected since late 1986 by the Rhode Island Cancer Registry. Drawing most of its data from inpatient settings and in-state pathology labs, Rhode Island incidence data for all cancer sites together are about 95 percent complete, with high reliability for essential variables. However, melanoma incidence statistics from the Rhode Island Cancer Registry, like melanoma statistics from most other non-SEER state cancer registries, are believed to be very incomplete. Melanomas which are diagnosed and treated in ambulatory settings and whose pathology specimens are sent to out-of-state labs may be missed entirely. (Given the importance of tracking the incidence of potentially

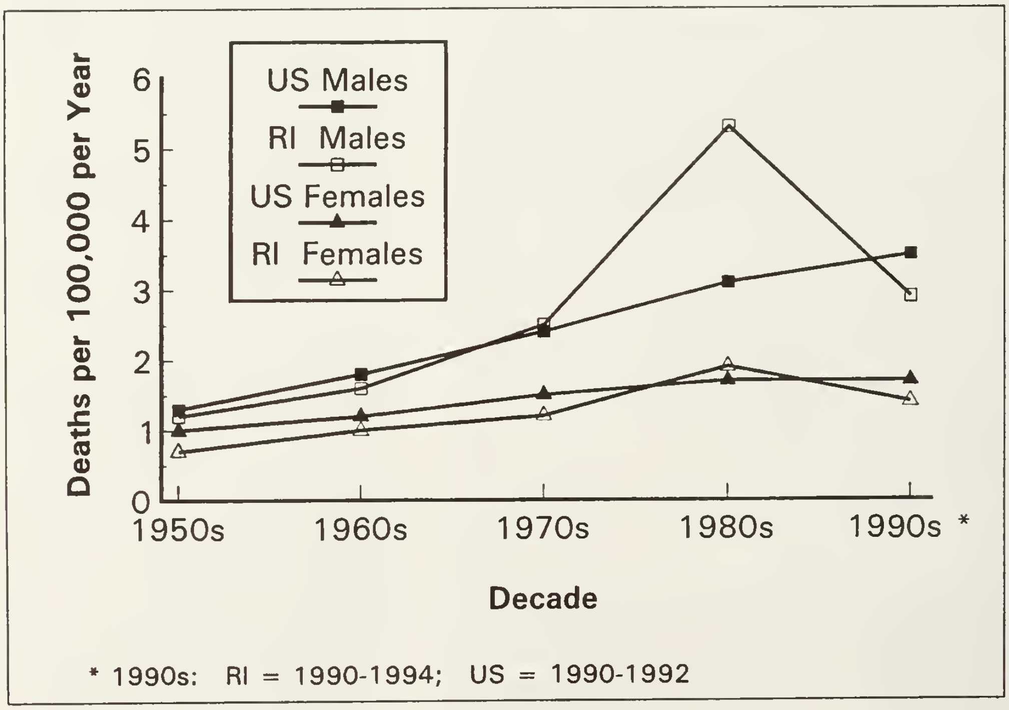

Figure 1. Annual Average Age-Standardized Mortality Rate for Melanoma of the Skin; Whites, Rhode Island and the United States.

fatal skin cancers, in future it may be necessary to request direct case reporting from physicians who treat melanoma in ambulatory settings or who refer specimens to out-of-state labs.)

Melanoma incidence in Rhode Island may be estimated using SEER data by multiplying age-standardized incidence-to-mortality rate ratios from the SEER system with age-standardized mortality rates from Rhode Island. The use of rate ratios for this purpose has been studied carefully, and is considered to be a reliable estimation technique, based on the observed stability of the ratios.[4] Rhode Island estimates of age-standardized melanoma incidence are slightly lower than comparable SEER incidence rates for both white males (16% lower in Rhode Island) and white females (18% lower in Rhode Island; Figure 2).[3] The age-standardized incidence of melanoma in both geographical areas is substantially higher among white males than white females (41% higher in the U.S., 43% higher in Rhode Island), a phenomenon consistently observed in national data.

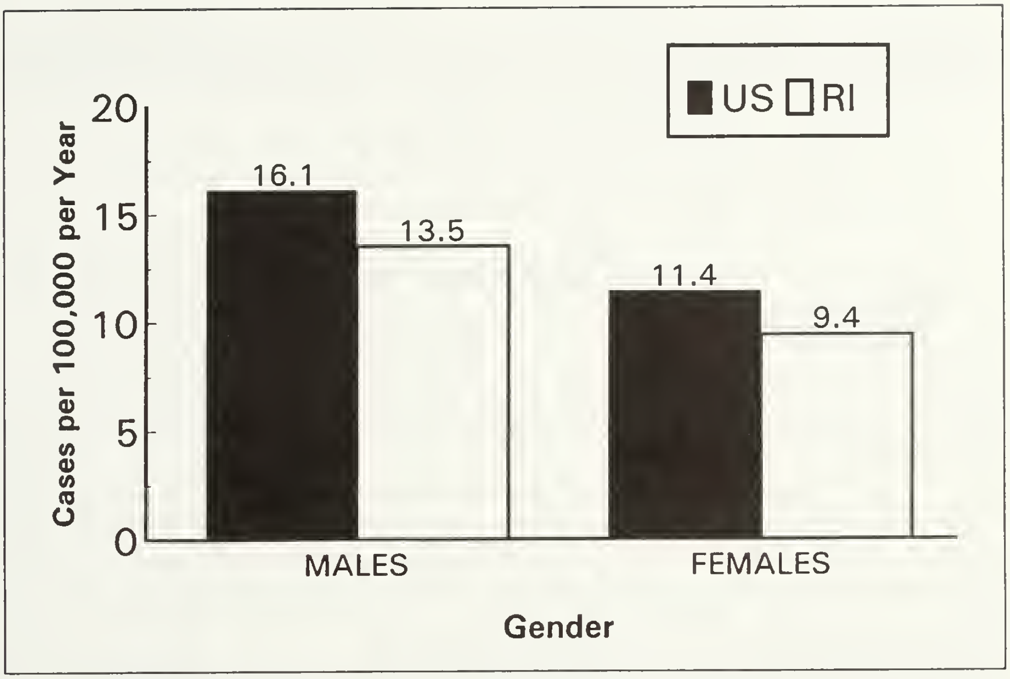

Figure 2. Annual Average Age-Standardized Incidence Rate for Melanoma of the Skin; Whites, Rhode Island, 1990-1994, and the United States, 1990-1992.

Effective prevention and control of melanoma incorporates two strategies: promoting the reduction of sun exposure to prevent the onset of melanomas, and skin examination to detect melanomas as early after disease onset as possible.[5] Both strategies are most efficient when directed at people with established risk factors for malignant melanoma, including:

- Clinical evidence of melanocytic precursor or marker lesions
- Large numbers of common moles
- Immunosuppression
- A family or personal history of skin cancer
- Substantial cumulative lifetime sun exposure
- Intermittent intense sun exposure or severe sunburns in childhood
- Freckles
- Poor tanning ability
- Light skin, hair, and eye color[6]

The rise in mortality from melanoma in recent decades indicates that the prevalence of one or more of these risk factors is increasing. Accordingly, a national panel has recommended: "Clinicians should remain alert for skin lesions with malignant features (i.e., asymmetry, border irregularity, color variability, diameter > 6 mm, or rapidly changing lesions) when examining patients for other reasons, particularly patients with established risk factors ... Appropriate biopsy specimens should be taken of suspicious lesions."[6]

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PUBLIC HEALTH BRIEFING

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by John P. Fulton, PhD

Proposed Skin Cancer Screening Recommendations

Rogers C. Griffith, MD, and John P. Fulton, PhD

OBJECTIVE

The Rhode Island Department of Health assembled an Expert Panel on Cancer Screening to advise the Department on revising the State's current cancer control plan, published in 1989.[1] After reviewing the current screening recommendations of national organizations and the most recent pertinent literature, the Panel proposed a recommendation for skin cancer screening to be incorporated in a revised cancer control plan scheduled for community review in December, 1996.

Current Recommendations

Organization	Recommendations
U.S. Preventive Services Task Force	• Does not recommend for or against routine screening for skin cancer by primary care providers. • Suggests that clinicians remain alert for skin lesions with malignant features, particularly patients with established risk factors for skin cancer. • Recommends to consider referring patients at substantially increased risk of malignant melanoma to skin cancer specialists for evaluation and surveillance.
American Cancer Society	• Recommends monthly skin self-examination for all adults and physician skin examinations every 3 years in persons 20 to 39 years old and annually in persons 40 years or older.
American Academy of Dermatology	• Recommends regular screening visits for skin cancer.
National Institutes of Health Consensus Panel	• Recommends regular screening visits for skin cancer. • Recommends that some family members of patients with melanoma be enrolled in surveillance programs.
Canadian Task Force on the Periodic Health Exam	• Does not recommend for or against routine screening for skin cancer by primary care providers. • Suggests that total skin examinations for a very select subgroup of individuals at high risk of malignant melanoma may be prudent.
American Academy of Family Physicians	• Recommends complete skin examination for adolescents and adults with increased recreational or occupational exposure to sunlight, a family or personal history of skin cancer, or clinical evidence of precursor lesions.
American Medical Association	• Does not recommend for or against routine screening for skin cancer by primary care providers.

Proposed Rhode Island Recommendations

- Do not recommend for or against routine screening for skin cancer by primary care providers.
- Clinicians should remain alert for skin lesions with malignant features (i.e., asymmetry, border irregularity, color variability, diameter > 6mm, or rapidly changing lesions) when examining patients for other reasons, particularly patients with established risk factors, including clinical evidence of melanocytic precursor or marker lesions, large numbers of common moles, immunosuppression, a family or personal history of skin cancer, substantial cumulative lifetime sun exposure, intermittent intense sun exposure or severe sunburns in childhood, freckles, poor tanning ability, light skin, hair, and eye color.[2]
- Recommend to consider referring patients at substantially increased risk of malignant melanoma to dermatologists specializing in skin cancer for evaluation and surveillance. Persons at substantially increased risk for malignant melanoma include those with melanocytic precursor or marker lesions, e.g., atypical moles [also called dysplastic nevi], certain congenital nevi, familial atypical mole, and melanoma syndrome.[2]

METHODS

- Review current skin cancer screening recommendations of national organizations.
- Review the most recent literature pertinent to skin cancer screening.
- Discuss.
- Propose a skin cancer screening recommendation for the State's cancer control plan.
- Write a simple rationale for the proposed skin cancer screening recommendation.
- Invite comments on the proposed recommendation with rationale.

RATIONALE FOR PROPOSED RECOMMENDATIONS

When the State's current cancer control plan was being developed in the late 1980s, the committee charged with this task determined that there was insufficient evidence to recommend for or against routine skin cancer screening of asymptomatic persons by health care providers. Since that time, little new information has become available to change that position. The relevant literature has been summarized by the U.S. Preventive Services Task Force[2] as follows:

- The vast majority of skin lesions (over 95%) are either basal cell or squamous cell carcinomas. Both "are high treatable and rarely metastasize." The case fatality of these lesions is low. About 2,100 annual deaths result from over 760,000 annual cases.
- The effectiveness of early detection for reducing mortality or disfigurement has not been demonstrated for basal cell or squamous cell carcinomas. There is no evidence that basal cell or squamous cell carcinomas detected by screening are more amenable to treatment and cure than those which present clinically.
- The accuracy of skin cancer screening by health care providers other than dermatologists is low.

Nonetheless, clinicians and their patients are urged to remain alert for the clinical manifestations of skin cancers, especially those which may prove to be malignant melanoma, a far more dangerous cancer than either basal cell or squamous cell carcinoma. Furthermore, consideration to refer patients at substantially increased risk of malignant melanoma to dermatologists specializing in skin cancer is recommended because:

- Screening by dermatologists for malignant melanoma appears to reduce the thickness of tumors diagnosed; survival is related to the thickness of tumors at the time of diagnosis.
- The accuracy of screening for malignant melanoma is greater among dermatologists specializing in skin cancer than among general dermatologists.
- The burden of malignant melanoma (incidence and mortality) is growing steadily. The case fatality of malignant melanoma is much higher than the case fatality of basal cell or squamous cell carcinoma. About 7,200 annual deaths result from about 34,000 annual cases.

COMMENTS?

We invite your comments on the proposed recommendation and rationale. Please send them in writing to Dr. John Fulton, column editor either by fax (401-861-5751) or mail (Rhode Island Department of Health, 3 Capitol Hill, Providence, RI 02908-5097).

Rogers C. Griffith, MD, is a Pathologist-in-Chief (Acting) at The Miriam Hospital.

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Vital Statistics

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health
Edited by Roberta A. Chevoya

Rhode Island Monthly Vital Statistics Report
Provisional Occurrence Data from the Division of Vital Records

Vital Events

	Reporting Period		
	May 1996	12 Months Ending with May 1996	
	Number	Number	Rates
Live Births	1,140	14,018	14.1*
Deaths	854	9,635	9.7*
Infant Deaths	(6)	(95)	6.8#
Neonatal deaths	(6)	(73)	5.2#
Marriages	835	7,740	7.8*
Divorces	358	3,576	3.6*
Induced Terminations	437	5,475	390.6#
Spontaneous Fetal Deaths	75	1,126	80.3#
Under 20 weeks gestation	(72)	(1,076)	76.8#
20+ weeks gestation	(3)	(50)	3.6#

* Rates per 1,000 estimated population
# Rates per 1,000 live births

Underlying Cause of Death

	Reporting Period			
	November 1995	12 Months Ending with November 1995		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	265	3,346	335.8	4,443.5
Malignant Neoplasms	208	2,491	250.0	6,402.0
Cerebrovascular Diseases	46	645	64.7	542.5
Injuries (Accident/Suicide/Homicide)	32	331	33.2	6,366.0
COPD	29	409	41.1	407.5

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.
(b) Rates per 100,000 current estimated population of 996,325
(c) Years of Potential Life Lost (YPLL)

Note: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

THE RHODE ISLAND MEDICAL JOURNAL

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NINETY YEARS AGO

[NOVEMBER, 1906]

Charles W. Stewart, a Newport surgeon, discusses the treatment of ulcers of the stomach. He notes, first, that the medical profession has but recently begun to appreciate the immense importance of this lesion which, he says, is encountered in about 5% of all autopsies. In the past gastric ulcer may have been called gastric catarrh or nervous dyspepsia. He stresses that hyperacidity [by HCL] is the basis for the mucosal lesion. Heightened lactic acid in the stomach, on the other hand, reflects a gastric stasis with abnormal bacterial fermentation. In contrast, he observes, there is usually no hyperacidity in gastric cancer. Nonsurgical treatment consists of a regimented diet [high in egg albumen] and rest. This form of treatment results in a cure rate of about 64% and an additional 18% substantially relieved. But, he warns, within five years about a third of those cured will have shown recurrence of the ulcer. He then describes some of the complications of non-surgical intervention including hemorrhage and perforation. Finally, he provides the readership with a detailed compilation of his own cases treated surgically the great majority of whom were "permanently cured." He details some features of his operative technic and urges that surgery rather than medical therapy be advised in peptic ulcer.

The *Journal* presents a summary of a symposium on appendicitis.

Donald Churchill, MD, discusses the history and biology of the disease noting that the first recorded case of appendicitis was published in 1759 by Mestivier. An 1824 paper by the French physician, Louyer-Villermay first defined the inflammatory nature of the disease and claimed that it presented certain unique clinical features. During the next five decades there was much debate as to whether the lesion existed at all, and if it did, whether it was centered in the appendix [appendicitis] or in the neighboring cecum [typhlitis.] The Boston physician, Reginald Heber Fitz, is credited with the first comprehensive description, both clinically and pathologically, of this common disorder. Finally the author summarizes many of the compiled series in the medical literature, listing also operative results. He notes that the first appendectomy in Rhode Island was performed by Dr. Collins on February 6, 1893 [the patient was discharged as cured after a 44 day post-operative inpatient course.] The author then discusses the role of such factors as abdominal trauma, indigestion, menstruation and the presence of ingested foreign bodies. The author concludes: "There are still unwritten chapters on the history and etiology of appendicitis."

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The diagnosis and prognosis of appendicitis are summarized by Dr. Arthur Hollingworth. He states that in the majority of cases the diagnosis is readily reached. "A previously healthy individual seized with acute general abdominal pain, with nausea and vomiting and perhaps a chill, and having the later localization of pain and tenderness over McBurney's point." And, finally, a white count in excess of 15,000 and fever insure the diagnosis. Success, in the author's judgment depends on three factors: a timely diagnosis, an early operation and an experienced anesthesiologist.

Dr. Herbert Terry presents the minority point of view that occasional cases of acute appendicitis do not require surgery and will recover under a more conservative treatment regime.

Finally, Dr. Jacob Rutherford outlines the surgical treatment of appendicitis. He states that there are approximately 134,000 cases of appendicitis in the United States, each year. He then summarizes the surgical experience from such clinics as Mayo and Ochsner showing mortality rates varying from 1% to as high as 17.2%. The time and character of the surgical intervention are carefully detailed, providing the reader with the varied views of the more experienced surgeons of the country.

FIFTY YEARS AGO

[NOVEMBER, 1946]

The lead article, written by Charles Bradley, MD, discusses the medical management of the convulsive child. After a brief consideration of the varieties of convulsive phenomena, Dr. Bradley outlines the steps toward complete treatment. He stresses the importance of careful neurological examination to rule out potentially dangerous disease which may require neurosurgical attention. He notes that medical therapy should be adequate to control the seizures but not so excessive as to supress the patient's personality or personal efficiency. The importance of "facilitating the child's social adjustment" is stressed. And finally, he declares that the physician not neglect the guidance of the child's parents, family and teachers.

Hugh E. Kiene, MD, discusses the office and hospital treatment of neuropsychiatric disorders. Amongst other interventions, the author defines the guidelines for the use of insulin shock and electro-shock therapies.

The *Journal* continues its policy of publishing the names of those physicians leaving the armed forces and returning to the civilian practice of medicine.

The lead editorial is a lengthy discussion of the history and fundamental philosophy of osteopathic medicine and whether or not it is a suitable form of therapy for prepaid third party reimbursement.

TWENTY FIVE YEARS AGO

[OCTOBER, 1971]

Abnormal serum alkaline phosphatase results are discussed by W.C.Griffiths, PhD, H.F.Martin, PhD, and S.J.Grivers. They describe a method [involving a heat inactivating procedure] which distinguishes skeletal from hepatic disorders as the source of an elevated serum alkaline phosphatase.

Elia Shammas, MD, describes the recent history of psychiatric day care centers in the state hospitals of Rhode Island. Such centers were initiated in 1964. The author concludes that these ambulatory centers shorten the term of treatment for the typical mental patient. Moreover, once discharged, the patient is less likely than the inservice patient to be readmitted for further treatment.

Seebert J. Goldowsky, MD, while searching the microfilm files of the *Providence Daily Journal* for the year 1855, uncovers data to indicate that Martha Harris Mowry, MD, was the first woman physician in Rhode Island. Dr. Mowry was born in Smithfield, RI, in 1818 and educated in a succession of Providence and Boston private schools. Her early medical education was through apprenticeship with a number of Rhode Island practitioners; her MD degree was awarded to her by Philadelphia Allopathic Medical School in 1853. Part of the year she fulfilled the duties of professorship at the Female Medical College of Philadelphia, and part of the year she maintained a practice at 22 1/2 South Main Street, Providence. She passed away in 1899.

Robert V. Lewis, MD, describes the two early leaders of England's Royal College of Physicians - Thomas Linacre and John Caius. The article describes their activities in 16th century England, their medical education at Padua, their roles as advocates of medical humanism and their many friends including Thomas More, Vesalius, Erasmus and others.

The editorials discuss the future of organized medicine and newer guidelines for pharmaceutical advertising in medical journals.

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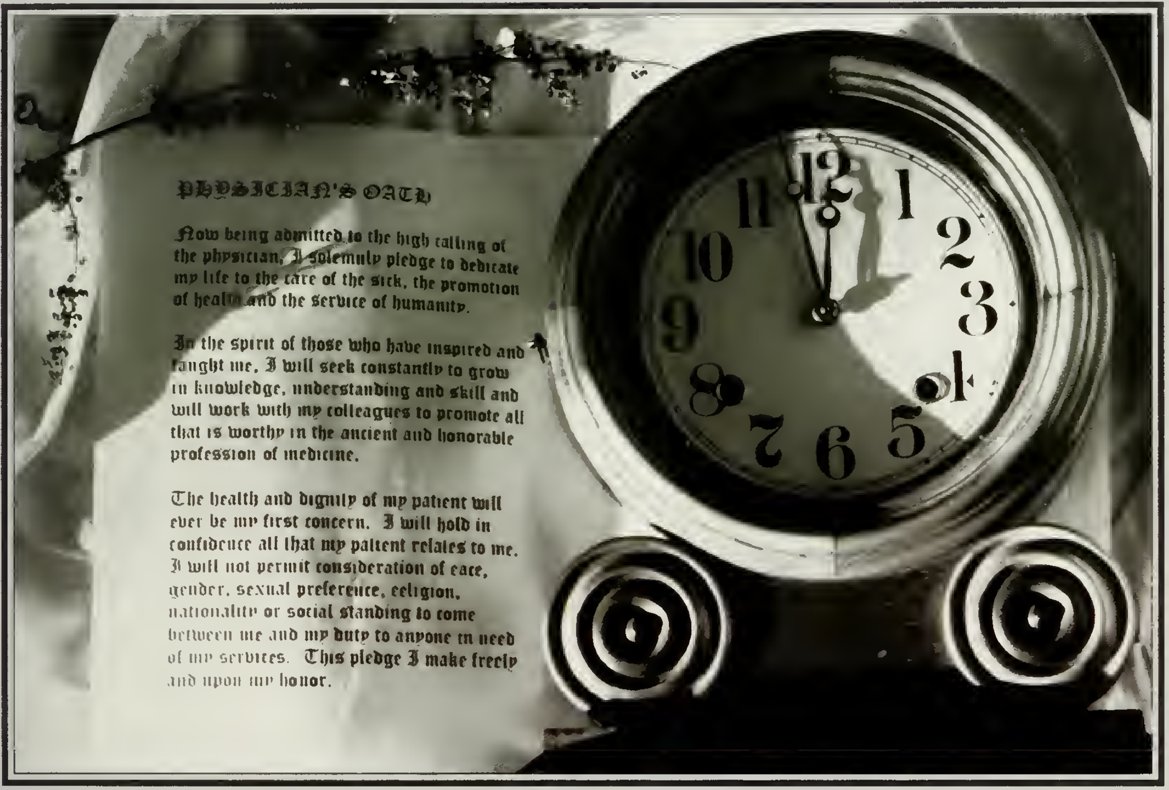

PHYSICIAN'S OATH

Now being admitted to the high calling of the physician, I solemnly pledge to dedicate my life to the care of the sick, the promotion of health and the service of humanity.

In the spirit of those who have inspired and taught me, I will seek constantly to grow in knowledge, understanding and skill and will work with my colleagues to promote all that is worthy in the ancient and honorable profession of medicine.

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Medical Students: Caring and Commitment in a New Era

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COMMENTARIES

Medical Students: Caring & Commitment in a New Era

Perhaps it was Aeschylus with the promise that time would teach us all things, that has led us to believe that eventually medicine would possess the answers. Still, as the calendar advances toward the millenium, few would argue that we know everything that we require. Hence, many of the current and future challenges will be addressed by the "newer" members of our profession.

This issue of *Medicine and Health/ Rhode Island* is devoted to student views on the direction of medicine. From the student response to Dr. Steven A. Schroeder's message in his 1996 Stanley D. Simon, MD, Affinity Group Lecture to student initiatives in the areas of gender equity, supporting families of children with disabilities, beginning a Community Health Advocacy Program, thanking faculty for the gift of their time and mentoring, and the creative sharing of feelings, the words of students poignantly tell us that they are ready to accept the gauntlet. Is this a new phenomenon? Not at all. Rather, as the lessons from Galen suggest, seeing the cycle of linkages renewed is both reassuring and a summons to maintain a sense of balance.

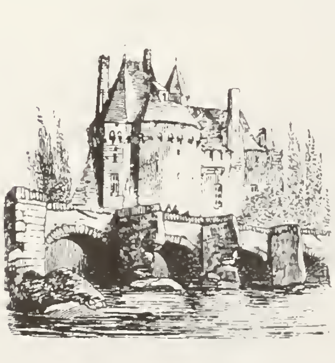
I want to take this opportunity to recognize and to thank the following colleagues, who have worked together with me in reviewing, selecting and editing the students articles for this issue of Medicine & Health/Rhode Island: Debra B. Abeshaus, Director, PLME Student Affairs and Office of Women in Medicine; Herbert Constantine, MD, Professor of Community Health, and Lucile Newman, PhD, Professor of Community Health.

– Lynn C. Epstein, MD

* * *

Scotland's Enduring Gift to Medicine

Prehistoric tribes took advantage of the natural protection afforded by the steep approaches to a prominent rocky hill on the Scottish plains just south of the Firth of Forth and established a succession of settlements upon its crest. For more than three centuries a Roman garrison then occupied this citadel as their principal northern outpost in the British Isles. When the Romans withdrew, the stronghold reverted to the local Picts who, in the year 617, were then conquered and displaced by Edwin, Saxon king of Northumbria. The Gaelic title for this site, Dunedin, was gradually supplanted by the name, Edwin's Burgh or, as it is known today, Edinburgh. The descendants of Malcolm then established their castle upon this rock eventually transforming a Midlothian frontier township of uncertain tenure to its present status as the first city of Scotland and, by the 15th century, as its capitol. It also became Scotland's cultural center, the home of Robert Burns, David Hume, Walter Scott, Adam Smith and Arthur Conan Doyle. But Edinburgh's most enduring contribution lies in the immense numbers of physicians that it provided for the expanding British Empire as well as for its innovations in the field of medical education, particularly that essential component of medical education called bedside teaching.



Long before formal medical education took root in Scotland, there were families of traditional healers in western Scotland; best known of these Highland families were the M'Beaths [sometimes spelled Macbeth]. Their rude treatises on folk healing, in Gaelic, are still preserved in the national archives of Scotland.

Prior to the 14th century Scottish scholars seeking sites for their education travelled to Balliol College in Oxford or to the continent. Because of an alliance with France, Paris became their preferred site for higher education in the disciplines of theology and law. The international ramifications of the Papal Schism of 1378-1417 created barriers for those Scots seeking overseas education, thus encouraging the creation of indigenous centers of learning on Scottish soil. St. Andrew's, the ecclesiastic capitol of Scotland, established the nation's first university in 1411; Glasgow, in 1451 and Aberdeen in 1494 followed suit. Somewhat belatedly, Edinburgh created a university in 1583, but in contrast to its three predecessors which were church run, Edinburgh's was fiercely secular. Following the Reformation, a decision was reached to modify gradually the four Scottish universities such that each might channel its limited resources into but one of the professional curriculums. And while some medical education persisted on the other campuses as an intellectual pursuit, to Edinburgh fell the task of establishing a formal medical faculty for the express purpose of training physicians.

During the 17th century, a poorly supervised form of medical education still prevailed in Edinburgh. The salary of only one professor [of anatomy] was provided by the City Council which also guaranteed access to the bodies of executed criminals for purposes of anatomic education. In 1670, a Physic Garden [ie, an herbarium] was assembled both to yield medicinals as well as to educate students in the art of applied botany. In 1681, through the urging of the local physicians, a royal chapter established a College of Physicians to create and uphold standards for the accreditation of new practitioners for the city. But a formal Faculty of Medicine was not fully organized and implemented until the year 1726 when Alexander Munro was appointed to the chair of anatomy and surgery. He then recruited four other physicians - all five trained in the medical school in Leyden, Holland, at that time Europe's leading medical school - to establish a functional medical faculty of Edinburgh. They transplanted to Scotland the principles of pragmatic, bedside-based medicine which they had absorbed from their great teacher Herman Boerhaave. Five years later, the City Council chartered the Royal Infirmary, to be attached to the medical school and designed expressly for supervised clinical education. Formal bedside education, a revolutionary concept in those days, became the abiding element of a demanding Edinburgh medical education. Indeed, this form of teaching became so popular that the hospital collected a regular fee for those many visiting physicans or students who "walked the wards." By 1738 chairs in botany, midwifery, surgery/anatomy, chemistry, materia medica and the theory of physic [ie, medicine] were fully operational.

The medical school in Edinburgh truly flourished during the latter half of the 18th century and was widely acknowledged as the world's leading center of medical education. In that interval it awarded 1,143 MD degrees to students from all over the world, including 195 men from the North American and Caribbean colonies. The MD degree from Edinburgh was not lightly or casually conferred. It required three intensive years of education, an original thesis as well as stringent oral and written examinations all conducted in Latin. At a time when most European and American physicians learned their art through indifferent apprenticeship, the rigorously educated graduates of Edinburgh naturally gravitated toward positions of leadership, particularly in medical education. The first medical school to be established in what would later become the United States began its operations in Philadelphia in 1765 under the inspired direction of Drs. William Shippen, John Morgan, Benjamin Rush and Philip Syng Physick, all Edinburgh medical graduates. Dr. Samuel Bard, also a graduate of Edinburgh, established this country's second medical school, in an institution later called Columbia University. Canada's premier medical school, McGill, in Montreal, was organized in 1843 by five Edinburgh-trained physicians. Other Canadian medical schools such as Dalhousie in Nova Scotia were consciously modelled after the Edinburgh curriculum. Until the mid-nineteenth century, Edinburgh remained the preeminent center of medical education attracting large numbers of Americans including Dr. Benjamin Rush, signer of the Declaration of Independence and Dr. Benjamin Waterhouse, a Rhode Island-born physician who later was a founder of the Harvard Medical School; and from the British Isles, such luminaries in non-medical fields as Peter Roget, Charles Darwin, J.S.Haldane and Arthur Conan Doyle. Only when the medical centers in Paris, Vienna and the north German cities offered comparable clinical facilities enriched further by basic research facilities in the emerging sciences of chemistry, physiology and microbiology did Edinburgh finally relinquish its leadership.

The influence of Edinburgh upon the practice of medicine in the English-speaking world cannot be overestimated. By 1850 65% of London's licensed physicians and 79% of physicians practicing in the English provinces were graduates of the Scottish schools of medicine. More specifically, during the years 1801 to 1850, while Oxford and Cambridge graduated 273 physicians the Scottish centers [principally Edinburgh and Glasgow] generated 7,989 physicians.[1,2] The list of those trained in Edinburgh looks like a compendium of medical eponyms: The Edinburgh trainees include: Addison, Bright, Hodgkin, Cheyne [and Stokes], Argyll Robertson, Kinnier Wilson, Colles, Cullen, Bell, Black, Percival, Corrigan, Mackenzie, Fothergill, Withering [of digitalis fame], Simpson [of chloroform fame], and Lind [of scurvy fame.]

– Stanley M. Aronson, MD

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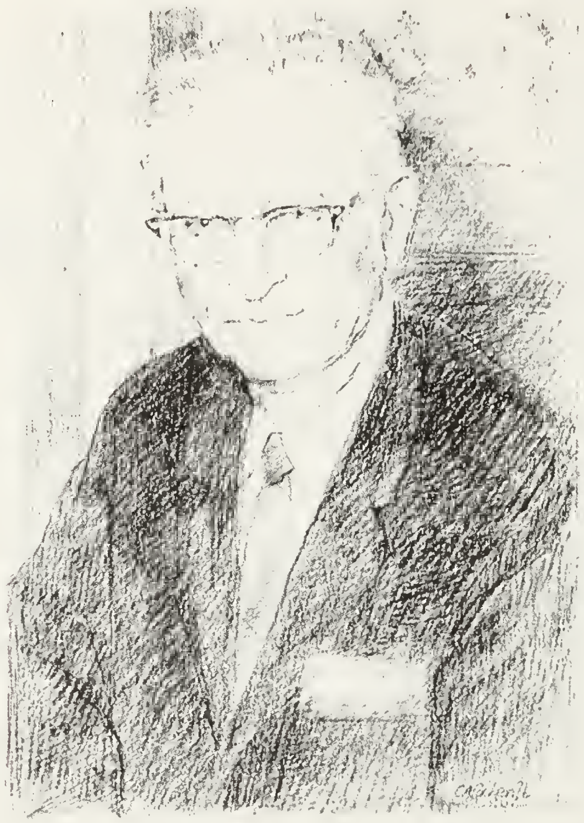

A Portrait of Stanley D. Simon, MD

Claudia Cockerill balances a dual career as the Affinity Group Program Coordinator for the Brown University School of Medicine and as an artist. She is a member of the Providence Art Club and the Warwick Art Foundation. This sketch was drawn from a favorite family photograph. It is both a tribute to the man "Stanley D.," and to his wife Marion and the Simon family, who have given so much to so many.

The Stanley D. Simon, MD, Affinity Group Lectureship

Dr. Stanley D. Simon (1916-1993) was born in New York City, attended Brooklyn public schools, Cornell University and Medical School. After serving in the Navy during World War II, he completed his orthopedic training at New York's Hospital for Joint Diseases and settled in Providence at the invitation of Dr. Carroll M. Silver with whom he practiced in what was the first medical partnership in Rhode Island. Over the next 40 years Dr. Simon demonstrated his devotion to his profession and his adopted community by serving as chairman of the Rhode Island and Providence Medical Societies, The RI Orthopedic Society (which he founded), the Rhode Island Medical Economics Committee and the Miriam Hospital Medical Staff. He was a member of the Providence School Committee, the Rhode Island Committee on the Humanities, the Trinity Repertory Company Board of Directors and the State Ballet of Rhode Island, of which he was chairman. Before his retirement in 1987, Dr. Simon served as Medical Director of the John E. Donley Rehabilitation Center in Providence.

In fond memory of his many contributions to the health of Rhode Island and of his oft-stated admonition to "treat the patient and not the disease," the Simon family, in cooperation with Dean Lynn Epstein of the Brown Medical School, established the Stanley D. Simon, MD, Affinity Group Lectureship. The principal paper in this issue is Dr. Steven A. Schroeder's Stanley D. Simon Lectureship address of January 30, 1996.

The Paradox of Medicine: Angry Physicians and Eager Applicants

Steven A. Schroeder, MD

Your generation of students, entering a health care world of great ferment, is facing an emotion different from my generation. It is one of anxiety about the wisdom of choosing your profession and whether that profession will bring the rewards that you will work so hard to enjoy.

At no time in the past fifty years have there been so many changes in the way medical care is financed and organized - or so much anxiety about what the future might bring.

Why have these changes occurred? There are basically two major reasons. First, as you know, expenditures for health care have risen at a rate two to four times the overall growth of the economy. Thus, more and more resources have shifted from other sectors of the economy into health care.

For example, in 1964, when I graduated from medical school, the nation was spending 5% of its Gross National Product on health care, or about $50 billion. Today health care is a huge industry, consuming 15% of the nation's resources, or almost one-sixth of the Gross National Product. In 1995 it is estimated that we spent a trillion dollars on health care. When you hear talk about reducing the growth of health care, it does not mean spending less money, but rather refers to slowing the rate of increase, so that it would take longer to get to 20% of the Gross National Product.

The second reason that health care is so much on the public's mind follows from the first. As medical care becomes more expensive, so does health insurance. The United States has long had a certain proportion of its population that does not have health insurance. It has tolerated this situation, although not with total comfort. However, as costs have grown and premiums for health care insurance have risen, coverage has eroded. Today, the majority of the uninsured population are members of working families, often in small businesses. People who *are* insured and lose their jobs in today's time of corporate downsizing also lose their health insurance. Others who wish to change jobs may find that if pre-existing conditions exist for them, their spouses, or children, a new job will leave them without health insurance. As a result of these factors, for the first time significant numbers of the working middle class are concerned that they may join the 40 million people who are already without health insurance.

Finally, government is a major payer for health care for the elderly and the poor, through Medicare and Medicaid. As you know, there is strong political sentiment to reduce the federal deficit - an action that will not be possible without slowing the rate of increase of the Medicare and Medicaid programs. Because of these phenomena - the fact that medical care is now big business, that the public is concerned that they will not be covered by health insurance, and that the government is a significant payer - health care has become political. I don't think there is any chance, in the foreseeable future, that this situation will go away. Thus, you are entering a career where, different from physicians in my generation, health care is and will remain a political issue.

In 1993 and 1994 there was - as you know - much debate about whether a national policy would emerge to assure health insurance coverage for all and to contain medical costs. It is common wisdom that the nation rejected such a solution. But in fact the reality is more complicated. While the United States has again rejected the prospect of providing health insurance for all, it has accepted - by default - a market solution to the problem of medical costs.

Thus, a surging private industry called managed care has been quietly growing and changing the way health care is financed and organized. Managed care has taken a number of forms, but the dominant ones have involved reliance on health maintenance organizations, as well as rigorous attempts by payers to manage the price and utilization of health care services. Because of the fact that most communities have an excess of hospitals and medical technologies, the pressure from payers is causing overall hospital capacity to shrink, thereby accelerating trends that shift medical care out of the hospital and into the office and community.

Change never comes easily to those affected, and many physicians today complain that things are not what they used to be. For example, recent surveys of practicing physicians indicate that as many as 40% would not go to medical school if they had to do it all over again. Many of these physicians are telling their sons and daughters, and the friends of their sons and daughters, not to go into medicine.

There are many reasons for the unhappiness of today's physicians. Declines in income - real or threatened - are certainly one cause, particularly among specialists in highly competitive regions. Loss of autonomy is another, as increasingly third parties are intruding into ordinary clinical decisions, asking about such issues as where, when, and how long to hospitalize, and the choice of consultants. Thoughtful physicians are also concerned about the increasing commercialization of medicine, and what it might mean for the core values of what should be a healing profession.

Yet, it is a strange paradox that - despite these concerns - applications to medical schools have surged in the past seven years, and are now at an all time high. How can we explain this puzzle?

Many of the physicians who express unhappiness with medical care today complain that things are not what they used to be in the "good old days." Since I am of the generation that is nostalgic for the "good old days," it might be useful to turn the clock back a bit and scrutinize that period more closely. It is true that physicians graduating in the 1960's and 1970's had unprecedented opportunities for employment. At that stage the nation was prosperous and growing, medical care was seen as a valuable commodity, and the question was, "How can we get more of it?" Medicare and Medicaid were passed, and medical institutions and physicians began to get paid for work that, at least to some extent, had previously been charity.

But let's take a closer look at those "good old days." In my medical school class of 1964, there were 150 graduates. Only 6 were women, only 1 was African-American, and there were no Hispanics. My classmates who took internships and residencies in hospitals in the southern part of the United States went to work in hospitals that were segregated by race, because it was not until Medicare was passed that all hospitals were desegregated. Now I don't mean to imply that my generation of physicians was sexist or racist, although I do know some individuals who fit that description. The point is that certain things, that were accepted without question at that time, would be unacceptable today.

Most importantly, although it was only 30 years ago, we had many fewer tools at our disposal to try to help the sick. Let me give you two examples. When I was a third-year medical student, President Kennedy's third child, Patrick Bouvier Kennedy, was born prematurely. He was hospitalized at Boston Children's Hospital with the diagnosis of "hyaline membrane disease," now known as respiratory distress syndrome. In spite of state-of-the-art medical care, he died after three days. Today, there is a virtual 100% probability that he would survive. True, the hospital bill might be as high as $100,000, but the prognosis would be excellent. Second, if a woman in 1964 found a lump on her breast, she would undergo a biopsy under general anesthesia, with a resultant frozen section opinion as to whether or not the lump was cancerous. If it was cancer, she would have a mutilating radical mastectomy that she would discover only upon awakening. There would be no choice of alternative types of surgery, chemotherapy, or radiation therapy. This was the practice of medicine in those "good old days."

... recent surveys of practicing physicians indicated that as many as 40% of them would not go to medical school if they had to do it all over again.

I can't tell you how many patients of mine died when I was a resident from potentially treatable illnesses such as heart disease, because we were not able to detect disturbances in rhythm or treat adequately their heart failure. The spectacular advances in diagnostic and therapeutic technology, imaging, laboratory tests, different medications, and new modes of surgery have dramatically increased our capacity to treat illness. The new advances in genetic diagnosis and treatment will certainly alter the face of medicine in the 21st century, improving our ability to avoid or ease the huge burden of illness caused by genetic factors. And new approaches to public health, spurred by aroused citizens, have led to spectacular declines in cigarette smoking and the ravages it causes, drunk driving deaths, heart disease, and stroke. True, we had the hubris to boast that infectious diseases would soon be a thing of the past - little suspecting the emergence of HIV, drug-resistant tuberculosis, and the new viruses such as Ebola and Hanta. And true, we did not foresee the epidemic of violence that now stalks our cities. But even with these twin calamities of resurging infection and violence, Americans are healthier now than ever before.

Finally, even with the recent constraints on medical spending, the income of physicians relative to other workers is considerably higher now than it was 30 years ago.

So here is my answer to why young people today have not taken the advice of their fathers and mothers, their uncles and aunts. The answer has three parts.

First, what health care might have been like 20 or 30 years ago is irrelevant to today's young people. They didn't experience that period, and therefore they won't mourn its passing, any more than they mourn the passing of 29 cents a gallon gasoline or 5 cent ice cream cones.

Second, young people can look at other sectors of our nation's economy and conclude that - as turbulent as time might be - medicine is the only sector that will continue to grow in the years to come. They understand that medicine will be more secure than business, the law, architecture, teaching, or engineering - for example. One has only to look at what is happening to executives of such large companies as IBM, Xerox, AT&T, or the banking industry, to understand that health care is not the only field that is undergoing profound change.

Third, and I hope most importantly, you in the audience understand that medicine - of all the professional opportunities - offers the best chance to improve people's lives. No other field has the privilege of ministering to people who come to you because they are in pain, disabled, or because they are frightened. You will have the opportunity, as the old French saying so eloquently describes: "to cure sometimes, to relieve often and to comfort always." No other field can so effectively blend science and art in the name of helping our fellow human beings. As Carola Eisenberg wrote recently in *The New England Journal of Medicine*, "...the satisfaction of being able to relieve pain and restore function, the intellectual challenge of solving clinical problems and the variety of human issues that we confront in daily function will remain the essence of doctoring, whatever the changes in the organizational and economical structure of medicine."[1] So, to you who are considering medicine as a career, I would say it is still the best game in town.

Now let me close with two brief admonitions for those who do choose medicine. These cautions are particularly salient in the turbulent world that is likely to characterize medical care for at least the next decade. The advice is: avoid the entitlement trap, and keep your eyes on the prize.

Avoid the entitlement trap. More often that I would have liked, I have heard physicians - younger as well as older - justify self-serving behavior with the rationalization that, "I deserve this because I worked so hard." Usually this excuse justifies actions that enrich the physician or that constitute rudeness to helpless or indigent patients. Though physicians have certainly survived rigorous training - often at a huge economic sacrifice - they are by no means the only members of our society who deserve rewards. Indeed, compared with other important occupations such as school teachers, physicians have much greater pay, prestige, and opportunity. So remember, medicine is both a privilege and a trust. Avoid the entitlement trap.

The second lesson is to keep your eyes on the prize - to remember why you chose medicine in the first place. You face many hard years of education and rigorous training. There will be difficult days and nights ahead, and you will not only witness terrible suffering, tragedy, and death, but you will endure personal periods of profound depression, despair and fatigue as you struggle with the fundamental tragedies of the human condition. There will be joys as well, as you experience intimacies of the human spirit that few others are privileged to share. And you *will* cure some, relieve many, and - I hope - comfort all. Out of these struggles will come strength, as well as personal knowledge of yourself and your chosen profession.

You will be united by the central premise of medicine - the joining of the power of science to the compassion of caring in order to minister to people who hurt. That is the prize of health care, and it is that prize that you must treasure, both for the integrity of your career and for the health profession that you represent, no matter what organizational or financing changes are swirling about you.

So let me close by offering my heartfelt encouragement to all of you. You are considering fields that will allow you to do good, and to continue to grow for the rest of your lives - to learn more about the human race, about your chosen profession, and - perhaps most importantly - about yourselves.

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Steven A. Schroeder, MD, graduated with honors from Stanford University and Harvard Medical School. He trained in internal medicine at the Boston City Hospital, in epidemiology as a member of the Epidemic Intelligence Service [Centers for Disease Control] and in public health at the Harvard Center for Community Health and Medical Care. He has held faculty appointments at Harvard, George Washington and University of California, San Francisco. Dr. Schroeder has been President of The Robert Wood Johnson Foundation, the nation's largest health care philanthropy, since 1990. He continues to practice general internal medicine on a part-time basis at the Robert Wood Johnson Medical School, where he is Clinical Professor of Medicine. His two sons attend medical school.

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Student Responses to Dr. Schroeder

In his 1996 Simon Lecture, Dr. Steven Schroeder discussed the paradox of modern medicine: many young people are vying to enter the medical field, while many older physicians are dissatisfied.

Brown medical students Ari M. Blitz, Amit R.T. Joshi, and Mahesh P. Sardesai responded to Dr. Schroeder's comments. Blitz discusses the commercialization of medicine and its effect on the physician-patient relationship; Joshi presents some benefits of structural changes in modern medicine, namely primary care and preventive medicine; and Sardesai urges physicians and health care professionals to be vigilant advocates for patients.

The Questionable Ferment of Modern Medicine

Ari Blitz, Sc.B.

"In our present day when so great an emphasis is being laid on keeping people well by periodic health examinations and preventive medicine, all this about medical practice may sound very old-fashioned"- Harvey Cushing, *Consecratio Medici,* 1926

Without question, as Dr. Schroeder suggests, in some respects the practice of medicine has come a long way since the "good old days." It is possible in any period regarded as the good old days to pick reasons why medicine would be more attractive in our own age. Gone are the days of leeches and operations without the aid of anesthesia, and the age when patients would routinely die of infected wounds. One does not have to look terribly far back beyond the twenty or thirty years ago that Dr. Schroeder has picked as his version of the good old days, to find medical practices so comparatively primitive that they do not seem to belong in the same century as their modern counterparts. There is no doubt that the rising egalitarian mood among medical professionals and improved techniques for treating disease make medicine in those respects more attractive today than ever before, just as a medical student or doctor twenty years ago could point to startling progress before that time. But progress must be made on all fronts.

Dr. Schroeder admits that thoughtful physicians are worried about more than their incomes. Indeed the physicians with whom I have spoken view the current changes in health care as an assault on the profession of medicine, not because of declining salaries, but rather because the very doctor-patient relationship seems never to have been so singly in jeopardy. The human aspects of medicine which have made its practice so attractive to generations of physicians are increasingly regulated by insurance providers directly or indirectly. The new emphasis on cutting cost in medical care has created pressure to shorten the interaction between physicians and their patients. The ability of the modern doctor, as Dr. Schroeder puts it, "to relieve often, and to comfort always" seems in danger of being sacrificed to the bottom line. Recently, the exposure of gag rules by insurance companies has highlighted the need for careful scrutiny of the power of insurance companies in determining the content of a physician's advice. If the above two examples are in any way indicative of a trend in medicine, then we ought to be horrified.

No one has suggested tossing out the thirty years of technology created in the interval since Dr. Schroeder's graduation from medical school, or suggested that the social progress within the field should be rolled back. Great advances have been made of which the members of the medical profession can be justifiably proud. What is more at issue is whether current changes in the health care system are sound in other than the economic sense. What really ought to be at issue is whether HMOs and other cost-managing strategies improve patient satisfaction. It is my belief that had the topic of commercialization been explored in the Simon Lectureship, the paradox (between increased professional dissatisfaction and more medical school applicants) to which Dr. Schroeder refers, which is very real, would have been seen more as a challenge to a new generation of physicians rather than an invitation to complacency. The quality of the doctor-patient relationship ought to be viewed as equally vital to patient care as the accuracy of diagnosis. Perhaps it is old fashioned of me, but I believe it is incumbent on those of us within or about to enter the medical profession to see that neither aspect of the practice of medicine is sacrificed.

Ari Blitz graduated from Brown University with an Sc.B. in Neuroscience. He is a first year medical student at Brown University School of Medicine.

The Prospects for Tomorrow's Doctors

Mahesh P. Sardesai

Regardless of the altruistic intentions of young physicians today, the doctors of tomorrow will have to become acquainted with management and organizational issues if they hope to contribute their talents effectively to society. Medical school curricula in the "good old days," as Dr. Schroeder refers to the 1960's and 1970's, lacked this training. As the emerging realities of medical practice in the 1990's and beyond become more obvious, medical training must adapt to prepare students adequately for the practice of medicine. Today's physicians can rest assured that medical schools are responding to this need. A quick perusal of almost any medical school catalog reveals many new opportunities for students to learn the ethical and economic ramifications of their chosen profession.

Dr. Schroeder rightly observes that health care has become a heated political issue in recent years and that public concern is unlikely to wane in the near future. Physicians may interpret the entry of third parties into the patient-physician relationship as a serious affront to their autonomy, livelihood, and security. Whether this perception is justified or not, physicians should take note of this trend and become increasingly active to support the welfare of their patients, who may easily be lost in the bureaucratic shuffle. Change in the system is inevitable, but it does not have to be harmful, especially if doctors can influence the manner by which it unfolds. At the same time, doctors must guard against becoming excessively radical; above all, they must never forget that regardless of the economic climate, their primary responsibility is to the patient. By becoming more prominent in the decision-making process at the organizational, local, regional, and national levels, the next generation of physicians can secure for their patients (and consequently themselves) some of the benefits which may otherwise be left for politicians and insurers.

A case in point is the issue of uninsurance, which Dr. Schroeder mentions briefly. It is common knowledge that hospitals in this country cannot deny urgently needed care to patients because of their inability to pay; in fact, many uninsured people seek their care in emergency rooms because they cannot afford normal office visits. Consequently, the problem of uninsurance is not so much an issue of the health care system failing to meet its commitment to patients than one of misallocation of resources. An increasing emphasis on preventive care and health education, encouraged in part by the desire of managed care providers to trim long-term costs, will likely help alleviate this problem to some extent. Tomorrow's physicians, who are becoming increasingly aware today of the long-term economic benefits of health promotion, can and will be proactive in this endeavor. Their efforts will likely be supported by legislation that makes medical care more accessible to presently underinsured and underserved populations, regardless of whether universal health care takes hold in this country.

On the whole, our nation's rising generation of physicians should be considered well-prepared for the challenges that face them. Perhaps the paradox that Dr. Schroeder describes should not be construed as illogical or unsettling. In spite of the complicated nature of the medical industry today, thousands upon thousands of high school and college students still consider medicine their dream career. The current surplus of medical school applications should comfort those who long for the practice of medicine to remain in essence a humanitarian calling. These students are knowledgeable about the complex realities of the health care setting today, and they are determined to become a part of that system tomorrow. They should be encouraged to use their training and talent to improve the system of health care delivery ultimately for the benefit of their patients.

Mahesh P. Sardesai is a junior concentrating in economics at Brown University. He is co-head of the campus-based Student Health Advisory Board and a teaching/research assistant in the Department of Community Health.

The Optimism of Modern Medicine

Amit R.T. Joshi

Dr. Schroeder touches on some of the changes that medicine is undergoing and the discontent it is creating among an older generation of physicians. His optimism is appropriate, however, given the positive ramifications of these changes. Managed care and primary care were curse words a few years ago. Now, after a few years of impartial and fair analysis, more and more physicians are beginning to acknowledge the benefits of such concepts as managed and primary care.

Certainly one of the most dramatic changes in modern medicine has been the financial restructuring of the health care delivery system through the introduction of managed care. Since it has impacted the way medicine is practiced in America to such a large degree, managed care is often the institution most readily scapegoated by disgruntled physicians of our parents' generation. Medical students today, however, having benefited from courses in medical management, health care economics, and government health policy, realize that managed care is a viable solution to the chronic problem of an overburdened system funded with limited resources. Managed care attempts to alleviate this problem through rational (albeit economic) allocation of those resources so that the greatest number of people might be served. Preventive medicine and primary care are two of the most important byproducts of the shift to managed health care.

Preventive medicine is a result of simple cost benefit analysis and common sense. It is based on the premise that sickness prevented now is easier (and cheaper) to cure than sickness left to fester. As a result of such forward thinking, more Americans are living healthier lives, eating better, exercising regularly, and living simply. Indeed, lifestyle and outlook are no less tangible to health than genetics and blood pressure. The great education drive undertaken by our nation's managed care physicians and organizations improves not only health, but can impact on the social fabric of Americans. The integrity of a strong family structure and support network can dramatically reduce illness and morbidity. Indeed, years from now, we and our patients shall reap the immense benefits of the willingness of managed care systems to invest in early prevention. Similarly, the institution of primary care as the workhorse of the managed care system is having a positive impact on the practice of medicine. Primary care physicians are able to gain intimate knowledge of their patients as whole people. This knowledge comprises the patient's psychological, personal, financial, familial, and professional makeup. Such an informed patient-doctor relationship can only make for more effective care and healing. Primary care physicians are regaining their position in society and among families as pertinent advisors on physical and emotional health.

With these changes, one realizes why programs like the Brown Program in Liberal Medical Education are so well thought-out and effective. Physicians are not technicians, and "curing" an illness is not like repairing a car. Accordingly, the education of physicians should not be limited by being purely technical. At Brown, students are trained to be humanists well versed in human philosophy and thought, social scientists able to understand the structure and problems of society, and healers with a firm understanding of the ailments of the common man, in addition to having a firm grasp of the scientific basis of the life processes. Biochemistry and physics are as important as literature, history, and language, for while the former teach us skills we shall use in medical intuition, the latter teach us about the people we hope to help.

Amit R.T. Joshi , a senior P.L.M.E. student at Brown University , is concentrating in classics and music. He is a member of the "Managed Care" Affinity Group, which is studying the efficacy of education in reducing inappropriate emergency room use.

Student Remarks at the 1996 Affinity Group Faculty Recognition Dinner: Remodelling Collaborative Learning

Ari Meir Blitz, ScB

The Affinity Group Program is one of the great assets of Brown's Medical School and the faculty who participate go above and beyond the call of duty to make it successful. As the only student present tonight I would like to thank you for your efforts on their behalf. At Dean Epstein's request I have prepared a few brief comments on changes occuring within the Affinity Group Program.

We are trained from our earliest schooling to work individually- collaborative work is scorned. Yet this collaborative work is exactly what the Affinity Group asks students do. Perhaps we should not be surprised then if some of the faculty present today have at some point experienced frustration when their groups seemed mired, like many committees in the real world, in circular argumentation, failing enthusiasm, or any other factor which can lead to an impasse in their progress. Dr. Lewis Thomas, the popular writer on medicine and biology, once wrote that the basic unit of life is not the molecule, not the cell as many of us have been taught, nor even the organism- the basic unit of life is actually the committee. If we were to venture to some far-away planet, that is what we should really look for with our sensors: traces of alien committees. The Affinity Group is modelled roughly on this basic unit of life.

Dr. Thomas approaches committees in his essay as an odd and interesting sort of social interaction. He describes them as being almost like a mating ritual: "when committees gather, each member is necessarily an actor, uncontrollably acting out the part of himself, reading the lines that identify him, asserting his [or her] identity. This takes quite a lot of time and energy, and while it is going on there is little chance of anything else getting done." Though Thomas was writing in jest; still, there is something in what he writes which cannot fail to hit home. It is a fact of life, though not always a popular one, that we often must work in groups. Medicine is not a monastic profession- though its ancient origins are religious.

Thomas's comical description of committees aside, many affinity groups have been slow to get started. Some of this getting to know one another is unavoidable, and at any rate highly desireable. Contrary to what Thomas suggests, our committees, the affinity groups, do become productive. However, recently we (the student senate and Dean Epstein) decided that we would like to make this start up time more efficient by making the goals clearer. It is too easy for the group to lose momentum before it has begun if the process of introduction to the experience takes too long. The first semester or two can be frustrating for students and faculty alike. Perhaps to some extent this has been the result of students, presented with something that resembles closely a course in the ordinary, traditional sense (including classmates and a professor) almost instinctively waiting for someone else to lead. They keep waiting for the curriculum.

What we have asked the rising juniors to do this year is design their own affinity groups. If they designed their groups, they would recognize that the success of their experience will depend not only on how well they interact with faculty members, but on their own efforts interacting with each other.

The students first met with us and brainstormed topics. We then grouped the topic areas together into eight broad areas and asked students to rank their preferences. We used this to match them with a group of other students with similar interests. At the next meeting the eight or so students in each group spent two hours talking to each other about their goals for their own affinity group experience. Collectively they wrote preliminary descriptions which are being used to recruit faculty members and a medical student fellow to the groups. All the groups seemed enthusiastic and some of the descriptions are creative.

We expect this description, like descriptions in past years, to be somewhat plastic. What is important about this change, however, is that we hoped when we set out to deliver students with more enthusiasm to faculty, students who have spent time together thinking about the benefits they might derive from the groups. In addition, the faculty member will now be able, before meeting the group, to get a sense of the students' expectations. We hope this will lead to a more satisfying experience for both parties.

The changes that are taking place make explicit the established, implicit goals of the program. Foremost among them is that students take an active part in shaping their own educations and learn to work with others.

By asking students to work together from the start to design the blueprint for their own affinity group experience, we hope to "jump start" the activities of each affinity group. We also hope to reinforce the responsibility that each student has for his/her own experience and the experience of the rest of the group

In another essay from *The Medusa and the Snail* Dr. Thomas points out the clear precedent in the natural world for organisms to work together, many so closely like the medusa and the snail that they reach a point of mutual interdependence. From this vantage, his comments on committees take on a more serious tone. The affinity group at its best is an experience where students and faculty learn more from their collaboration than they might have singly – a sort of intellectual symbiosis. The ideal graduate of the Affinity Group Program is able to communicate to his or her peers and participate in group decision-making more effectively, increasing a fundamental skill in the profession. I hope that the Affinity Groups will continue to be a model of well functioning committees and productive social interactions.

Ari Meir Blitz, ScB, is a first year medical student at Brown University. As an undergraduate, he was coordinator of the P.L.M.E. Senate and, later, the P.L.M.E. Senate Affinity Group Liaison. More recently he had a summer research assistantship to assist with the development of an Affinity Group Manual.

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Promoting Greater Understanding: Pairing Medical Students with Families of Children with Disabilities

*John Susa, PhD, William Hollinshead, MD, Peter Simon, MD,
Mehri Brown, MD, Kerith Davidson, BS, Carolyn Greene, BA,
Darissa Kon, BS, Jennifer Lane, BA, Delia Radovich, BA, Erica Reed, BS,
Linda Shiue, BS, Beth Toolan, MD, Adeline Winkes, BA*

During the last 25 years, improvements in both neonatal life support technology and medical/surgical interventions in conditions which had previously resulted in early childhood mortality have resulted in a dramatic increase in the numbers of children and adults with severe disabilities. The increased advocacy, during the same period, to assure that these individuals remain in the mainstream of our society, instead of being institutionalized, means that many more physicians will come into significant contact with patients with severe disabilities and/or their family members.

The Brown University School of Medicine Affinity Group Program provides an opportunity for some medical students to explore in depth a medicine-related topic identified by the common interest of the faculty and student members. Each affinity group consists of six to ten students and two to three faculty members (physicians, scientists and other health care professionals). Our affinity group was designed to help medical students learn about families of children with varying degrees of ability. This was accomplished through a variety of activities including group discussion, guest speakers, review of relevant literature and primarily by the longitudinal linkage of individual students with families of children that have significant disabilities. This experience made it possible for students to observe the impact of disability on the development of the child, the family responses to the child and the disability/handicap-related challenges, as well as societal responses to these challenges.

By having a variety of contacts with families of children with significant disabilities, physicians-in-training learned important lessons about their future patients, as well about themselves. During the four years that they spent with "their families," they were learning about the resilience and dignity of people who face major challenges imposed by significant disabilities. These experiences also helped them recognize that nonbiologic factors and value systems significantly influence the lives of patients with disabilities as much as or more than biological factors. At a personal level these students could recognize personal values concerning their approach to patients with disabilities and chronic illnesses. These physicians-in-training recognized personal strengths and limitations relevant to their practice of medicine, and found ways to increase competencies in areas of identified weakness.

The physician's role in helping patients and families cope with challenges is critical. The longitudinal experiences gave the physicians-in-training the opportunity to explore these changing roles and bring them into contact with some of the complex real life needs of these families as well as some service providers and advocates who are supporting their assigned families.

Comments from students and parents highlight the impact of these experiences.

FROM STUDENTS:

"Having a member in my immediate family who is disabled has made me especially appreciate Dr. Susa's affinity group. I've been with the group for three years and each year I've learned so much. The first year we were assigned families who had children with severe disabilities. I must admit, I felt very wary and anxious. Luckily we were all well prepared by several discussions about what it meant to be different, our own perspective of self and others and other topics. The highlight of my three years has been meeting a medical student with cerebral palsy. This solidified in my heart that disability is merely a misnomer; it says nothing about ability."

"Visiting families of children with disabilities has really shown the resiliency found in human beings. Although their children did not initially fill their views of what a 'perfect' child would be, the parents are completely devoted in their love and care for all their children, 'perfect' or not. Their lives, though faced with unforeseen complications, are lived with complete acceptance and unconditional love."

"I joined this affinity group, after a year of working with children, living in abject poverty, who had chronic asthma and parasitic infections. I came hoping to gain a better understanding of disabilities which are more visible, and unlike asthma and poverty, irreversible. I was matched to a family of a child with cerebral palsy. I found this contact to be very thought provoking. The mother shared her experience of the joys and difficulties of giving birth and raising a child with a severe disability. Her frank discussion of the process of growing from accepting her child to loving her, moved me to wonder how I would react in the same situation. Just as we can learn from people with disabilities, we can learn from their parents. I hope to gain skills to make me both a more competent physician and a more nurturing parent."

"I have had a wonderful experience visiting a very young child with Down syndrome as well as cardiac and respiratory problems. I am very grateful to him and his mother for opening their home to me and allowing me to see many aspects of their private lives; while teaching me about the daily management, financial, and social aspects of living with Down syndrome."

"This year I visited a family with three children and many pets. Two children are deaf, one also has significant respiratory difficulties and the other is otherwise healthy. The third child is not medically involved. I really appreciate how willing this family has been to help me learn more about the human side of medicine. It has been especially fascinating for me, as I have a special interest in the use of American Sign Language and the culture of the deaf."

"Although the child I visit has autism and does not interact in the traditional way, my experience with him and his family has been particularly broadening. The opportunity to observe and to learn how a family adjusts to a daily challenge is something that I doubt I will encounter in regular medical school classes. I hope I have been able to bring a measure of reassurance to this family that many doctors are interested in learning about their particular situation and problem."

"No one can tell M.'s parents that their child is of average height or weight or intelligence for her age, but averages ceased to have meaning in M.'s family long ago. What is more important is the fact that even though M. can't find her way into the expected ranges for head circumference, fine motor ability or cognitive staging and has no place within the definition of "normal", she has found a place within the classroom, her Sunday School and her family. For M.'s distinctly remarkable parents have chosen to ignore diagnostic labels and fill the lack of expectations given their child with goals and ambitions they deem appropriate. What's more they've succeeded in making others—teachers, physicians, etc., accept these goals also. And so ...I'm left wondering, among the many questions that have arisen for me in these first few month of getting to know M. and her family: why must parents who have a children with a 'disability' (M.'s parents cringe to hear that word associated with their daughter) fight to offer their children what others are given freely?"

"Through my affinity group, I have had the privilege of visiting a single working mother, R., with an only child who has severe developmental disabilities. I have witnessed their daily routine and discussed the cultural issues which have made it difficult for the mother's family to accept her child. I have been astounded by R.'s statements like 'I am more dependent on my daughter than she is on me,' considering that T. is completely dependent on her mother. Her mother is an attractive woman, but her social life is extremely limited because of her obligations to her daughter. She does not seem to mind. On the other hand, I have seen R. in times of total despair, when she was ready to give up and felt that she could no longer provide her daughter with adequate care. I felt helpless and left their home wondering what I could have done or said. To my surprise, I received a phone call from R. at 6:00 A.M. the next morning. She wanted to thank me for listening because she felt much better, and that she just needed to get things off her chest. This was the first real experience which reminded me why I chose to go into medicine."

> *... disability is merely a misnomer; it says nothing about ability.*

From the parents:

"Having Brown University medical students come to my house to learn from me and my child makes me feel great. Who would have thought that someone like me with only a high school diploma would be helping to train doctors!"

"We have had lots of doctors who knew about their specialty and how it related to my daughter's health care needs. Very few of them, however, understood how it related to her day-to-day life. I hope that the students that go through this affinity group will know more about how disabilities affect all aspects of a person's life. I think they will be better doctors if they do."

"Although our child does not have any serious special health care needs, our pediatrician has been very helpful to us in helping get our daughter the educational services that she needed. Doctors are listened to, while parents are often not. I have tried to let my student know how powerful she can be when helping special needs children."

"I have learned a lot about how my son's disability affects his life. I also have had to learn about his medical problems. Sometimes I have questioned some of his doctors' decisions because I was concerned about their impact on my son's non-medical needs. Some doctors didn't mind, but I could tell others were not very happy. I don't think doctors should be upset when parents question things that affect their family's lifestyle. I'm trying to help my student learn that parents know a lot and that a well informed, and assertive parent can be a partner not necessarily a problem."

Conclusion:

Maximizing the effectiveness of the physician as a member of the health care team for children or adults with severe disabilities requires that physicians-in-training understand the far-reaching impact of disabilities (restrictions in functional capability imposed by physiology) and handicaps (restrictions in functional capability imposed by social context) on the life of their patients and families. Physicians will also need to be more familiar with the impact of interventions available to the health care team. Since the outcomes of intended interventions are an improved quality of life, those outcomes must be measured against the societal values of independence, integration, productivity and inclusion which define quality of life.

Because most physicians have little experience beyond the clinical arena with the lives of people with disabilities, the chance to see the important ramifications of interventions on the lives of patients and their families helped students increase their competency in recognizing and managing the social and community contexts and impact of health care. The long term informal contact between these physicians-in-training and families also helped students establish the kind of rapport that needs to exist if an effective therapeutic relationship is to be established between them and their patients with disabilities. This is the foundation of patient-physician communication. The personal impact of these experiences as expressed by some of the students attests to the fact that there has been some important introspection that has led to greater self-awareness and personal growth.

The competency-based curriculum of the Brown University School of Medicine (*MD 2000*) focuses on nine core abilities. Our affinity group provided opportunities for physicians-in-training to improve on three of those abilities: Effective Communication; Self-awareness, Self-care and Personal Growth; and The Social and Community Contexts of Health Care.

John Susa, PhD, a member of the faculty of the Department of Pediatrics, is the Director of Family Support for the University Affiliated Program of RI, a multi-university training program that prepares professionals who provide service to people with developmental disabilities. He and his wife are parents of two sons with developmental disabilities.

William Hollinshead, MD, a member of the faculty of the Departments of Pediatrics and Family Medicine, is the Director of Maternal and Child Health of the Rhode Island Department of Health.

Peter Simon, MD, a member of the faculty of the Department of Pediatrics, is the Director of Programs for Children with Special Health Care Needs of the Rhode Island Department of Health.

Beth Toolan, MD, an affinity group Fellow for three years, is a 1995 graduate of the Brown Medical School. Mehri Brown, MD, an affinity group Fellow for one year, is a 1996 graduate of the Brown Medical School.

Kerith Davidson, Darissa Kon, Jennifer Lane, Erica Reed, Linda Shiue, and Adeline Winkes are Brown University PLME students who have completed the second year of training.

Carolyn Green and Delia Radovich, who entered Brown Medical School as post-baccalaureate students, have completed their second year of training.

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The Community Health Advocacy Program: Changing the Relations Between Communities and the Medical Campus

Deborah Archer, AB

ABBREVIATIONS USED

CHAP	Community Health Advocacy Program
NJMS	New Jersey Medical School

The Community Health Advocacy Program (CHAP) is a wonderful new opportunity for students interested in health care to join with Providence community members in providing health education and improving access to health care services in Rhode Island. Founded in September 1995, CHAP was funded through an Echoing Green Public Service Fellowship and partially through a Learn & Serve grant from the joint efforts of the Howard Swearer Center for Public Service and the Brown University School of Medicine. The program evolved out of an idea created by a small group of undergraduate and medical students in the 1994-95 academic year. We sought to initiate a program that would allow the integration of health care with a needed public service. After a year's worth of interviews and informal assessments we found that many communities do not receive proper health care due to a variety of barriers to available services. Barriers include nonexistent or insufficient insurance coverage, unemployment, language differences, mistrust of the medical community and varying cultural beliefs regarding health care. While many medical and social services exist to assist these individuals, they are not utilized. In an effort to address the situation, CHAP was established: to minimize roadblocks to health and social services through education and to help others find the tools they need to live healthy lives.

In 1995- 96, after receiving the Echoing Green Fellowship, I began to develop CHAP further. The program established two sites, an advisory board, and co-founded the Providence Family Van project. In addition, CHAP worked to implement a service-learning component within a first year medical school course at Brown. The Community Health Advocacy Program emphasizes education as a key factor in providing preventive health services. The design of the health education is tailored to each community with their participation so that their needs are sufficiently met.

CHAP is a collaboration of students, community leaders and health professionals. The program offers preventive services and educational outreaches determined by collaborating community sites and student health educators. The student health educators work with community representatives and local volunteer physicians and nurses. Teams of students are assigned to a community site, where they work throughout their one-year commitment to the program. Their roles include designing educational outreaches with referrals, and organizing an annual health fair for their sites. Volunteers are asked to commit approximately 4 hours per week for one year to the program. The volunteer program is modeled after the New Jersey Medical School's (NJMS) Community 2000 program. The NJMS has developed a partnership with Brown University School of Medicine; CHAP is one product of that collaboration.

A CHAP site is an organization or group that wishes to have some preventive health education and gain some resources and referrals regarding their access to health care. The two sites developed in 1995 are East Side Apartments, and Mount Hope Day Care Center, Inc., both in the Mount Hope Neighborhood adjacent to Brown University. The East Side Apartments is a low-income, mostly senior citizen's high rise, where CHAP works with residents on basic health, nutrition, exercise and other health information of the residents' choice. At the Day Care Center we work with teachers in developing and supplementing their drug and alcohol curriculum for 3 to 9-year old children.

The CHAP advisory board consists of site participants and members of their respective organizations as well as other community members, community health organizations, and local academic health institutions. CHAP also co-founded with Women and Infant's Hospital the Family Van project - a collaboration of CHAP, community organizations, such as Dorcas Place, International Institute and the Minority Health Collaborative, and Women and Infant's Hospital. The Van is a mobile health education unit, dedicated to providing education and preventive care through screenings for blood pressure, glucose, pregnancy, and lead.

> *"The Community Health Advocacy Program is a collaboration of students, community leaders and health professionals."*

Personal Reflections on CHAP

Overall this was a successful, productive year. There were many challenges, both programmatic and personal. First, was the overall development of the program while simultaneously managing the volunteers and sites. I wanted all involved, from the advisory board to the volunteers, to feel ownership of the program. That required incorporating everyone's ideas while maintaining a level of organization. The challenge also remained to keep the volunteers and communities motivated for workshops when the process of developing workshops and recruiting participants was slow. Interacting with community and gaining trust was another challenge but a welcome one. At first the mention of Brown University and the medical school closed doors; however, persistence and listening to community demands was our road to success, but explaining this to volunteers who were eager to start yesterday was difficult. I feel the road has been paved, so that approaching communities with requests and receiving requests for health education programs will be easier in the future.

Personally this was a rewarding and soul-searching project. I embarked on this journey to understand why I wanted to enter medicine. My studies had always focused on education. My question was: why be a physician? and how does it relate to education? It did not take long for these questions to be answered loud and clear. Through working with students, professionals and community, I saw the importance of education and health. There is a need for health care professionals to have those intrinsic qualities of patience, trust and understanding which make a good teacher. I saw the need for the communities to have health care professionals who took the time, as a teacher would, to explain their conditions, to work with them to overcome their illness or simply to encourage them to stay healthy. After working with Mount Hope Day Care Center and East Side Apartments I now know it is not only my dream but is necessary that I enter the medical profession, to continue the work of CHAP and affect change socially, politically and personally.

Summary

Both CHAP and service-learning are unique new additions to medical education. The Medical School, Swearer Center for Public Service, and the Providence community have shown tremendous support and commitment. This commitment continues with the medical school's hiring of the Service-Learning Coordinator, who will help direct CHAP and organize service learning opportunities for medical students. CHAP provided me with an incredible learning experience, both frustrating and empowering. I was able to make sense out of medicine in the context of community health and also help others make sense of why an understanding of the communities in which they work and live was important to their medical education. On the whole I am pleased with the work and progress of CHAP as well as the service learning. I look forward to its future success and the newly forged partnerships of participating communities and the Brown Medical School campus.

Deborah Archer, AB, a first-year medical student, concentrated in educational studies (Brown '95). She founded the Community Health Advocacy program and is a recipient of a National Health Service Corps scholarship.

Preventing and Responding to Sexual Harassment and Sexual Assault
[A Resource Guide for Medical Students]

Kathleen Hogan, BS, Yvonne Mark, AB, Reshma Paranjpe, ScB

Editorial Note:

Last spring, to address a need identified in an Office of Women in Medicine survey of Brown medical students, Kathleen Hogan, MD '99, Yvonne Mark, MD '97, and Reshma Paranjpe, MD '99 - members of an Ad Hoc Committee on Gender Equity of the Office of Women in Medicine - volunteered to write a resource guide for their peers on sexual harassment and sexual assault. The students wanted to create a document that condensed the relevant information available at Brown.

The student-authors consulted with a variety of individuals, including Mr. Samuel Ramirez, Director of Brown's Equal Employment Opportunity/Affirmative Action Office, Ms. Toby Simon, Director of Student Life on campus, and Ms. Barbara Tannenbaum, Ombudsperson, as well as the American Medical Women's Association, the Rhode Island Rape Crisis Center, the Brown Police and Security, and the Providence Police Department.

In sponsoring the guide, the Office of Women in Medicine aims to increase awareness about sexual harassment and sexual assault, and, most importantly, to provide a network of support for medical students and the Brown Medical community. Toward prevention, one goal is to make more explicit concerns about language and behavior that constitute microinequities in our treatment of each other.

Lynn C. Epstein, MD, Associate Dean of Medicine for Student Development and Women's Affairs; Debra B. Abeshaus, Director, PLME Student Affairs/Office of Women in Medicine

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Abridged excerpts from *Preventing and Responding to Sexual Harassment and Sexual Assault: A Resource Guide for Medical Students:*

"Underlying all teaching is an assumption that both teacher and student are entitled to respect for their dignity as human beings. This idea is a fundamental part of the social contract that binds us, and it is especially important at Brown because of the high value we attach to the quality of teaching. When a teacher violates a student's dignity, an environment of intimidation and fear is created. Such intimidation is demeaning, violates the professional code of conduct, and compromises effective learning. It can also progress into criminal behavior. Because medical students interact with a number of professionals — residents, graduate students and nurses — in addition to the faculty, opportunities for abuse abound.

Most members of the Brown community respect the dignity of others, and in so doing help to maintain the high educational standards we set. There are some, however, who abuse the trust placed in them, and mistreat students. This treatment, when it occurs, often takes the form of sexual harassment. Students may find it difficult to confront, report, or extract themselves from abusive situations because medical school requires a fixed schedule of courses and clerkships, and because students' success depends largely on their teachers' evaluations.

The School of Medicine will not tolerate mistreatment or sexual harassment of its students. Because medical education takes place in a large network of sites, ... the School depends on students to report ...mistreatment. This manual is a laudable effort to inform students how to respond to treatment they find abusive or harassing. I endorse its aims and support its recommendations...."

– Donald J. Marsh, M.D.
Dean of Medicine and
Biological Sciences
April 2, 1996

"Harassment of medical students, residents, medical school faculty and administration, and patients or other members of the community we serve, by groups or individuals on or off the medical school campus is a growing problem. Harassment includes, but may not be limited to, overt or covert threats to individuals or groups, acts of violence, intimidation, defacement of personal or public property, intolerant behavior, or neglect to respond effectively to such incidents. An environment that permits harassment ... impairs the educational mission of the medical school and the humane mission of the health care profession. Acts of harassment cannot be tolerated..."

– Statement on Addressing Threats and Acts of Violence Directed at Members of the Academic Medical Community, AAMC, 1996

The purpose of this handbook is two-fold:

First, we offer options if you feel that you are being mistreated or harassed by students or professors in the classroom or in the hospital.

Second, we provide information about sexual assault and a step-by-step "How-to" guide for dealing with its aftermath.

PART 1: SEXUAL HARASSMENT

What is Sexual Harassment?

Sexual harassment is a form of sex discrimination forbidden by the School of Medicine, and prohibited by state and federal laws. It is about power and the abuse of power, not just about sex. Sexual harassment is defined at Brown as:

- unwelcome sexual advances;
- requests for sexual favors;
- other unwelcome verbal or physical conduct of a sexual nature where:
- such conduct has the effect of unreasonably interfering with an individual's welfare, academic or work performance, or creates an intimidating, hostile, sexually offensive education or work environment;
- submission to such conduct is explicitly or implicitly made a condition of an individual's academic success or employment; or
- submission to or rejection of such conduct is used as the basis for academic or employment decisions.

MYTH: Sexual harassment affects only a few people.

FACT: In a survey of medical residents in a training program, 73% of the female respondents and 22% of the male respondents reported one or more incidents of sexual harassment during medical school or residency (Komaromy et al, 1993).

MYTH: Sexual harassment only happens to women who are provocatively dressed.

FACT:Sexual harassment can happen to anyone, regardless of dress or gender.

MYTH: If the person had only said "NO," the harasser would have stopped immediately.

FACT: Many harassers are told "NO" repeatedly. NO is too often heard as YES.

EXAMPLES OF SEXUAL HARASSMENT

Unwelcome sexual advances

- uninvited touching, hugging, patting (note: second degree sexual assault occurs if a person's genital area or buttocks or a woman's breasts are touched.)
- threats or insinuations that a person's grade may be adversely affected by refusing to submit to sexual advances

Requests for sexual favors

- the suggestion of sexual favors in exchange for rewards

Other verbal, written or physical conduct of a sexual nature which may create a hostile environment

- graphic sexual commentaries about a person's body
- unwelcome use of sexually degrading language
- continuing flirtations or propositions when it has been made clear that such conduct is unwelcome
- obscene gestures or sounds
- written notes of a sexual nature
- consensual sexual relationships where such relationships lead to favoritism of a student or subordinate employee and where such favoritism adversely affects other students and/or employees

Is it Appropriate for Medical Students to Date Doctors in the Hospital?

According to Brown's Sexual Harassment Misconduct and Assault Prevention policy, faculty members and teaching assistants are advised against relationships with students. If one does date an instructor or another doctor within the hospital, your fellow students may view this as a potential conflict of interest, especially if the person whom you date is connected to the people who evaluate you. ...the decision to date someone who has authority over medical students should be made with careful consideration.

What Can I Do If I Think I'm Being Sexually Harassed?

Sexual harassment is hardly ever clear-cut. There are circumstances that may make us feel uncomfortable, but it is difficult to determine malicious intent. ...There are some things that you can do.

"My professor stares at me in class and offers to help me study. He/She makes me feel uncomfortable, but hasn't approached me outside of class or tried to touch me. I just want him/her to leave me alone!"

Speak up. The person may not realize the behavior is offensive.

Try to discourage the behavior. Dress and act professionally. Avoid the individual if possible.

Tell someone! Talk to friends, colleagues, or an advisor. Be aware, however, that an advisor may not be able to keep your concerns confidential. For example, if there have been repeated allegations against the same individual, a formal investigation may be initiated, regardless of your intent.

Keep records. Write down what happens and how you responded. This is important if you decide to go to the administration.

Report behaviors on course evaluation reports.

Consider talking to the individual with a neutral party present. Or talk to the person's supervisor.

Write a letter, including 1) a factual account of events and dates, 2) a description of how it made you feel, and 3) a statement telling the person to stop the behavior. It might just surprise the harasser and make him/her stop for fear of a formal charge. However, be aware that writing a letter can lead to retaliation in grades or evaluations.

What if I Observe Behavior that is Inappropriate?

If you witness repeated, unwanted, and uninvited conduct by one individual toward another, or hear or see someone being propositioned, leered at, touched.... you may be witnessing sexual harassment. While you are under no legal obligation to do anything, you might:

- Ask the person you think is being harassed how you might be helpful.
- Consult the Ombudsperson or one of the other resources suggested in this handbook.
- Tell the person who you feel is being offensive about your uneasiness with her/his behavior.

What are my Informal Resources for Sexual Harassment Grievance Resolution at Brown University?

"One of the doctors I work with on my clerkship is consistently making sexual propositions towards me. I think it is meant as a joke, but it's not funny anymore. He/she also touches me at every opportunity. I am afraid to make an issue of this. I just want the behavior to stop. What can I do?"

Brown University has a policy for informal and formal grievance resolution (the 1994 Brown University Sexual Harassment, Misconduct, & Assault Prevention Policies and Procedures handbook).

In the case above, the student could contact a resource person to discuss solutions; e.g., writing a letter to the harasser, or using a third party intermediary.

The grievance allegations must be reported to the director of the EEO/AA.

Confidentiality will be respected as much as possible. However, it cannot be guaranteed. If there have been repeated allegations against the same individual or if the episode is of serious concern, a formal investigation may be initiated, regardless of your intent.

What are my Formal Resources for Sexual Harassment Grievance Resolution at Brown University?

I filed an informal grievance against one of my professors. The situation with the individual who has been harassing me is now worse.

In cases of severe allegations (e.g. rape, sexual assault), or when informal grievance resolution has not been successful,... a formal investigation should be requested. If the allegation is directed against a member of the Brown faculty, the Provost, EEO/AA, or the Faculty Executive Committee will investigate. The Brown Office of Student Life is responsible for hearing complaints regarding fellow students.

If the allegations are substantiated, formal sanctions will be imposed - ranging from a reprimand to separation from the university.

The formal grievance resolution process is a serious step. It is often difficult to prove sexual harassment. Investigators tell the individual of the allegations and he/she must respond in a timely manner. An attempt is made to keep the proceedings confidential.

What are my Options Outside of Brown University to Deal with Sexual Harassment?

In cases of sexual assault or rape, the Providence Police Department or the Attorney General's office should be notified.

If the sexual harassment occurs at one of the hospitals, another recourse is the hospital's Human Resource Director. if you report an incident to the hospital, they are obligated to investigate, and confidentiality cannot be guaranteed. Many of the doctors with whom you work are affiliated with Brown, and the Medical School can revoke their academic status.

PART 2: SEXUAL ASSAULT

What is Sexual Assault?

Many sexual assaults go unreported. Rape in particular is underreported: fewer than one third of college students whose experience meets the definition of rape would consider it rape. The following definitions have been paraphrased from Rhode Island General Laws (Title 11, Section 37):

First degree sexual assault, or rape is sexual penetration by any part of a person's body/ any object into the genital, oral, or anal openings occurring when there is (a) force or coercion or (b) mental or physical inability to communicate unwillingness to engage in an act, of which the accused is (or has reason to be) aware. Physical resistance or verbal refusal are not required to indicate lack of consent; for example, when the victim is asleep or drunk, he or she may be unable to give consent.

Second degree sexual assault is sexual contact (intentional touching of a person's genital area or buttocks, or a woman's breasts) under the circumstances defined above.

Sexual assault is not limited to rape. Non-consensual sexual contact involving coercion, intimidation, force or threats qualifies as assault, whether committed by a stranger, acquaintance, instructor, or friend. Approximately 85% of reported sexual assaults on campus are committed by someone the victim knows.

Unfortunately, medical students are vulnerable to unwanted sexual advances. According to a 1990 AMA Women in Medicine survey of 3rd-year medical students, half of female students experienced unwanted sexual advances.

Sexual misconduct is a crime under federal law, and is prohibited at Brown. Violators (students/faculty/staff) face disciplinary action including but not limited to separation from the University, permanent notation in their records, and/ or formal grievance procedures.

What Should I Do If I Have Been Raped?

Seek medical attention as soon as possible. Even if you are not injured, go to the nearest ER as soon as possible. Try not to bathe, brush your teeth, eat, change clothes or wash before you go to the E.R. Even if you have washed, it is still crucial that you be examined to document what has happened, and will be crucial in case you decide to press charges now or in the future.

An evidence exam should be done within 12 hours of the assault, preferably within 3 hours. Call a Woman On Call , a counselor from the R.I. Rape Crisis Center, or a friend to accompany you to the E.R.

What are my Options Outside of Brown University to Deal with Sexual Assault?

What if I decide to press charges for either rape OR second degree sexual assault?

You have two major options: inside and outside of Brown. You could pursue either or both options.

However, the accused will NOT have a criminal record if found guilty of a violation by the University disciplinary system.

For legal advice, the Sarah Doyle Women's Center and the Rhode Island Rape Crisis Center can provide lists of attorneys who deal with sexual assault cases.

What will happen to me at the ER?

A physician will examine you using a Rape Exam Kit. He/she will examine, treat, and document injuries, and collect clinical samples for testing and evidence. You may receive prophylaxis for STDs and pregnancy. You will be referred to a confidential rape crisis advocate.

What about confidentiality?

Your exam will be confidential; you do not have to press charges.

Criminal Prosecution

You can file formal charges with the Providence Police, leading to an investigation by the police and the Attorney General. A grand jury will determine whether sufficient evidence exists to take the case to trial.

Civil Suit

This involves seeking restitution of damages or expenses for the assault.

What are my Options WITHIN Brown University to Deal with Sexual Assault?

If the perpetrator was a Brown student, staff or faculty member, you can pursue disciplinary options within the University in addition to criminal and/or civil charges. If you have been raped, you should file a formal grievance.

What is the next step?

Formal investigating officials will hear the grievant, the accused, and witnesses. Grievances will be handled as confidentially as possible, with information available only for investigative or resolution purposes.

What will happen if the accused is found guilty of a violation?

Substantiated allegations will result in penalties ranging from reprimand to separation from the University with permanent record notation.

What if I am not satisfied with the outcome?

You can appeal the University's decision through the Provost.

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HIV

As the wheelchair stumbled into the room,
A heavy silence filled the air,
For the grave virus that has taken so many,
Had staked its claim for one more

Her face sat cocked to one side,
The soft palm supporting the pain,
Dejection and defeat screamed within,
As every system writhed in agony

The virus attacked the pancreas on that day,
Driving a stake through the abdomen,
Words hung to her lips, aching to leave
As only the ice of winter could free the answer

The sounds and images of a grandchild
Radiated across her face,
Breaking that melancholous aura
For just a brief moment,

Yet, no one could ever know the truth of the illness
For their igorance was a necessity,
Life is too burdensome to absorb another worry,
Especially one inflicted so carelessly

Soon the pain inside will pass,
Leaving Mrs. Jones to the care of her cousin,
Waiting patiently until the end,
When the hard truth will be known.

– Jeffrey R. Brown, AB

Jeffrey R. Brown, who received his undergraduate degree from Brown University, is a second year medical student. His poem was inspired by a patient interview conducted through the affinity group program.

Medice, Cure te Ipsum: Lessons from Galen

Lynn C. Epstein, MD

The literature on medical education cogently documents the evolution of medicine from an apprenticeship trade with scant factual underpinnings to the more information laden and technologically oriented profession of the day. [1-4] Not surprisingly, this maturation process has been marked at numerous points by the belief that a scientific epiphany has revolutionized care. While the continuing gains in medical knowledge and the accompanying ability of doctors to treat the sick have been real , the passage of time has too often proven the espoused remedies of one era to be of limited value or frankly harmful in the next. [4,5] Moreover, the presumption and often conviction with which physicians proclaim the worth of their treatments have been the basis for satire and chagrin. How much of what we embrace as truth today will suffer this fate over the ensuing decades?

Along similar lines, there is a parallel literature which chronicles the complex and changing relationship between the university and the medical school. [6-9] Thus, while early in this century the recommendation to ground medical school teaching in a solid undergraduate college foundation was a crucial reform, several decades later the strong emphasis on scientific and technological innovation has caused many to revisit the question of an appropriate place for the humanities and social sciences in the education of doctors. As the glut of available information threatens to overwhelm our medical school curriculum, what need have we for the "softer" behavioral sciences, much less for the broader realms of the university? As medical educators struggle to pare down classroom hours for students to manageable numbers, must one inevitably eliminate all but the mandatory core sciences?

Major organizations and specialties are calling for caring and empathic treatment by doctors , while common system reforms and practice demands increasingly ask doctors to have time-limited interactions with their patients.[9,10] On the eve of a new era, how can we best prepare our students to deal effectively with the challenges they will inevitably face?

At the Brown University School of Medicine, one paradigm which aims to balance the caring with the curing aspects of medicine is the Affinity Group Program, a small group, problem-based, educational and advising program. Drawing analogies between the system and the individual, the program assumes that preparation for the profession of medicine must proceed simultaneously in two domains: the professional and the personal which are described in detail elsewhere.[11,12] The focus here is on the interface between the advising and educational realms targeted within the program and within the Stanley D. Simon, MD, Affinity Group Lecture and Forum.

Education versus Training:

According to Webster's, training carries implications of standards of efficiency, which result from instruction, discipline and practice. The broader concept of education builds on the notion of schooling in preparation "for life or for some particular task." In other words, the *education* of medical students must be placed in the larger societal context and needs to include linkages across disciplines, cultures and sites. Students must master a knowledge base subject to continual expansion and revision, and, at the same time, must see beyond the narrow confines of medicine proper. This blend of humanism and science is a means to a better practice of medicine, both through better treatment of patients by doctors and a more fulfilling life for doctors.

A call for including more rather than less in programs for students is made with a clear awareness of the need for restraint and balance in the curriculum. Addressing the biological, behavioral, social and psychological aspects of illness requires a broad scope to thinking and scholarship. Our students must learn integrity, respect and compassion at the same time as they learn the content of medicine and strategies for remaining current. Or, put in other terms, while there is a need for the science or the knowing, there is also a need for the art or the living.

The Anatomy of Student Development:

The Affinity Group Program, which bridges the undergraduate and medical school years at Brown, has as a core goal student personal and professional development . Predicated on the assumption that there is a close relationship between the living and the knowing, the program treats issues of growth, ethics and responsibility as more than just background embellishments for the practice of medicine. By linking students with faculty in small problem-based groups around shared interests at a very early point in their education, the program builds on natural student feelings of empathy and desires to help others. The focus on fostering abilities in the areas of effective communication, problem solving, and personal growth provides a background to help students integrate what is learned in other courses. The Affinity Group provides a continuity experience in a safe environment, while it encourages reflection about the care of patients, the life of doctors and the practice of medicine.

By what means does the Affinity Group Program presume to aspire to such lofty goals? The answer is deceptively simple: by making the students *partners* in their own education. Within affinity groups, students shape the activities their groups will follow in pursuit of agreed upon goals. The program offers opportunities to integrate and to broaden students' experiences and to provide much needed mentoring. In this way, the program avoids the view of education as a process from without, where experts cause things to happen to passive students, and one which would leave little incentive for real student involvement. Instead, learning is collaborative, responsibility is shared , and students experience medicine directly, taking them beyond the image of science.

The term "student development" is meant to encompass more than the educational and advising experiences which take place over the course of pursing the baccalaureate and medical degrees. In this instance, the whole is greater than the sum of its parts. The personal transactions of students, their biases, values, ethical and moral development, those internal responses which together shape what will later be clearly manifested, i.e. language, behaviors and external manifestations, are crucial building blocks in professional development.

"Quod Optimus Medicus Sit Quoque Philosophus"

- Galen[13]

Against the backdrop outlined above, the Stanley D. Simon, MD. Affinity Group Lectureship and Forum provides a venue for all program participants to engage in thoughtful dialogue about the task and direction of medicine. An outgrowth of an earlier series on Health Care in the Year 2000, the mandate of the lectureship is specifically dedicated to furthering the personal and professional development of students in the medical program at Brown.

The inaugural Stanley D. Simon, MD, lecture took place in 1995 with a talk by Dr. Leon Eisenberg entitled, "Waiting for Godot: What to do Until Hugo Arrives," which examined the evolution of medicine from healing to science, from science to the biopsychosocial, and from a system of individual practitioners to networks of managed care organizations, sometimes more interested in money than in care. Dr. Eisenberg encouraged maintenance of "caring in the curing", in terms both of interactions with patients and system advocacy for them. In so doing, he focused on a central tenet of the lectureship: that student development is heavily predicated on attention to the greater needs of society. Service learning and social responsibility contribute directly to the well-being of individuals and organizations in the community. Just as it is said that "to teach is to learn twice (Joseph Jobber), so it can be said that helping others furthers the well-being of those who perform the service.

Building on this theme, the second Stanley D. Simon, M.D. talk by Dr. Steven A. Schroeder, "The Paradox of Medicine: Angry Physicians and Eager Applicants" was held in 1996. As can be seen from the text and the student responses in this issue, the lecture energized listeners to keep a balanced perspective towards the system changes in medicine, and to maintain the interest in helping others which brought them to medicine in the first place.

Returning to the initial question, what is our message to students? Our goal in raising such complicated, yet compelling issues is relatively modest: to raise questions, not to provide answers -answers that may only be partially accurate and time-limited. We should remember Alice's experiences in "Wonderland," in which the Gryphon commented on Alice's amazement at what she had seen, "That's the reason they're called lessons, because they lessen from day to day."[14] We can assist our students to prepare for real life challenges by helping them to frame questions, update their knowledge base and preserve their empathy, their caring and their core values.

As educators, mentors and colleagues, we need to maintain our humility; we do not have a monopoly on answers. While a personal bias of this author is on the value of broad interdisciplinary experiences, of the humanities and social sciences, this bias is tempered by an awareness that one can be literate and yet inhumane, and that philosophers can be intellectually correct yet isolated from real-life experiences.

Perhaps our obligation, to our students, our patients, our families and ourselves, is simply to be the best we can— the wisest, the most knowledgeable, the most caring and the healthiest. Our need to meet standards of excellence must be tempered by reality. After all, well-being is not just for others. All of us need to practice what we preach and in time, who knows what the most important lessons will be?

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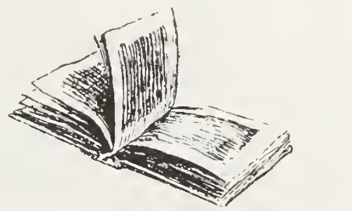

Point of View: A House Divided Against Itself: On Hippocrates and Swimming with the Sharks

Jean Plover, MD

> *"I swear by Apollo the Physician...*
>
> *To consider dear to me as my parents him who taught me this art; to live in common with him and if necessary to share my goods with him...*
>
> *I will prescribe regimen for the good of my patients according to my ability and my judgment...*
>
> *I will preserve the purity of my art, I will not cut for stone... I will leave this operation to be performed by practitioners (specialists in the art)..."*

Doctors represent medicine's hands as often as they do its heart. In the most practical terms, doctors know how to take care of patients and they spend almost all of their time doing it. If the manager of a ball club becomes frustrated with his players, he does not decide to play the game himself. We do not call a plumber to a fire or a fireman to a leaky faucet. But when the government tried to fix health care it was not the medical professionals whose counsel it sought. A focal, strategic and catastrophic error was made.

As issues of cost management and increased access were widely reviewed, it became clear that many subplots and political agendas were being played, and that consensus on the hows and whys of reform would not come easily. It also became clear that while physicians were in agreement with the mandate for reform, their vision for the direction that this reform should take, was seen as yet another of the "special interests" being represented. Rather than being viewed as having an essential, fundamental role in the analysis of how the system of health care could be "fixed", physicians were, by in large, assigned the designation of the culprits who had "broken" it and not included at the highest levels of policy formation and implementation.

Even if doctors were to assume responsibility for having had too sharp a focus on delivery of care at the expense of an adequate focus on cost , or for having been as a group unable to mount an adequate ethical response to the needs of every patient, insured or uninsured, they remained essential to any consideration of remedy.

But in losing sight of the core principles which drive medical practice, physicians were perceived by government as having too much of a vested financial interest in the outcome to be a reliable resource for the reform that it intended. A shift to a more purely "business" model emerged, and the American public began giving voice to new concerns regarding preservation of quality and choice. Yet despite the fact that no consensus regarding the nature, if not the need for reform had been reached, insurers began to accelerate the movement toward managed care *as if* by federal mandate and to justify radical restructuring of health care delivery based on this new "mandate". It was a presumption of advantage and control that would revolutionize the way the health care industry could be interpreted and driven. Cost savings became the mantra of the "emperor's new policy," and medicine began to be reshaped not by physicians but by insurers who were rapidly repositioning themselves for success and profit in the marketplace.

Insurers conceived a model whereby it would be possible to defend threats to their own huge profits and still be perceived as cutting costs, by circumventing the utilization of services by both physicians and patients and shrinking reimbursement to physicians. They did so while "shifting risk" to physicians, who remained exclusively responsible for outcome to the patient. Physicians who had traditionally been compensated for their skills and for the provision of services were now expected to cut costs and "manage risk" by rationing care. In the name of cost savings and "utilization review" insurers came between physicians and their patients by abrogating physicians' control over clinical decision-making. They introduced reams of paperwork and layers of non-physician overseers. They interfered with the doctors' right to determine what was medically necessary, where support was needed in consultation, and to whom referral could be made. They turned medicine upside down, shifting focus from provision of care to the concept of what care could be withheld. In so doing they subverted the most basic principle of the doctor-patient relationship, that of patient advocacy.

Doctors continued to take care of patients, but they were becoming increasingly fearful of the threat that this "management" would have on the quality of care that they could deliver and on their own vulnerability in an increasingly hostile marketplace where profit and loss consideration ran counter in many cases to patient advocacy. The message that "going along" allowed you to "get along" was clear. Managed care was presented as a fait accompli, an inevitable new reality that would demand a fierce loyalty or extract a heavy price. Sometimes that price was interpreted to be the loss of your practice. Managed care became a runaway train and the impulse to jump on was being based largely upon fear rather than well considered choice or the belief that this new system had provided us with a solution that was somehow visionary.

At the same time, insurer "oversight" with the paper work it generated and the attendant personnel demands it created significantly increased practice costs, making physicians even more financially vulnerable and insurer-dependent. Physicians felt pressure to work even harder and see an increased volume of patients more quickly to meet costs. The quality of the contact between doctor and patient was being externally manipulated and profoundly affected by forces over which they felt little control.

But of far greater consequence has been the nature of policy implementation which helped to insure that doctors *could not* respond in a collective voice to the egregious presumption of control over health care decisions by third party payers. Insurers created confusion, artificial division and introduced a "herald patch" phenomenon of health system reform.

Changes in the delivery of health care were imposed at different rates in different parts of the country in such a way as to "signal" inevitability and generate infighting and good guy/bad guy adversarialism among specialties. I do not believe for an instant that this was because insurers suddenly "got" the concept of Family Practice. In some areas, change was occurring so rapidly that physicians were left with consequences rather than questions and some fine physicians found themselves out of a job. State laws were already being drafted to deal with some of the most serious outcomes of this presumption of control by insurers, at a time when other states had little experience with the gag rules and advocacy deselection which drove this legislation.

As would befit the "emperor's new policy" there was also "phantom" change where health care systems appeared to respond with reactionary panic to changes that they feared but which had never even occurred. Hospitals, university groups, individuals' practices and specialties developed a circle-the-wagons mentality with a series of individual wagon trains moving as fast as they could toward whatever seemed like the best bet for survival, and then closing rank. Hospitals sought an answer to decreasing revenues in mergers and the control of physicians and their practices.

For those still relatively unaffected in the eye of the hurricane there were plenty of "experts" giving lots of conflicting advice. It became difficult for many physicians to know whom to trust and what to do next. Whatever was happening it was clear that it was not happening to all physicians in the same way at the same time. It is difficult to rally the troops if they have not all been brought into battle or are not even certain that they are fighting the same battle. It is brilliance to divide them to the extent that they do not even recognize that they are on the same side.

As a Family Physician I deeply believe in the best traditions of our specialty. I have practiced Family Medicine as a patient advocate, promoting prevention and early intervention, continuity of care and patient and family centered coordination of care. In my professional experience Family Physicians and subspecialists worked collaboratively and cooperatively in consultation together and shared the goal of excellence in patient care. Insurers are subverting the concepts of continuity and advocacy even as they pretend to promote them.

While medicine may have more than one face and differences among specialty groups exist, when medicine is functioning as it should, we are all working together in the best interest of the patient and are cognizant of our dependence upon and respect for one another. We are foolish if we fail to recognize what the sacrifice of the specialist to the insurance god portends. Will not our own substitution with midlevel providers become their next "solution"?

Family Physicians as case managers can provide an invaluable contribution to the coordination of care when, as in the case of a very sick patient, other specialists may be involved. But primary care physicians were never meant to be "trolls on the bridge" and a managed care system that promotes that model and would have us keeping patients from crossing that bridge when we determine they need to do so, presents a grave danger to us and to our patients and does a great disservice to all medical practitioners. Part of the skill in the practice of our specialty is the knowledge of when consultation is appropriate.

Insurers' interference in this judgment and the acrimony that it has created is motivated by interest in increasing their profits and keeping us divided. Seizing upon and exaggerating our difference just insures our inability to find a unified voice in defense of our profession and our patients.

Fear is not a good partner in decision making and insurers are keeping us fearful. Fear can deafen us to well reasoned arguments and profoundly narrow our focus. Fear can cause us to reject the best efforts of physicians "trying to bring us together to do the right thing" for the "safer prospects" of bigger more politically connected mergers. There are lots of doctors who aren't at all good at politics because they spend all of their time just trying to take care of patients. Shall we leave them all behind? Those who survive cannot only be those who can swim with the sharks. We will lose some of our best physicians that way.

If deals are struck that disregard patient interest, if we sacrifice those who do not comply with lower standards, if compassion is traded for promise of profit, it is the soul of our profession that we forfeit. If we fail to come together now, if we fail to clarify misconceptions, bring our own messages to the American people and restore public trust in our advocacy, we may lose the ability to do so altogether leaving insurers to determine what the face of medicine in the 21st century will be.

When I first came to Family Practice the face of Medicine for me was the Norman Rockwell painting of the elderly doctor, head askew, listening attentively, his stethoscope planted on the chest of a doll as his little patient looked on with concern. While medicine in the 21st Century may necessarily look very different from that wonderful print, must we lose sight of that vision of it altogether?

Whether we are solo or group practitioners, primary care or subspecialist, university or community physician, medicine must still be about taking good care of patients to the best of our ability no matter when, where, or by whom it is practiced. Physicians and not insurers must retain the right to make critical decisions about patient care because it is physicians who have been trained to do so and physicians who retain the moral, legal and professional responsibility to do so. Loss of control erodes the doctor-patient relationship, the core principles of medicine and the satisfaction which we derive from its judicious, compassionate practice.

All the while, brilliantly managed advertising campaigns place insurers squarely on the side of the angels. They are saving money, giving people what they really deserve and promoting physicians whose work they understand and support. Physicians have on the contrary become more susceptible to malpractice litigation as the disparity between insurers' marketing claims and managed care realities creates increasing dissatisfaction with provided care.

Even more important than consideration of liability, we are, as physicians, still driven by the same sense of responsibility for the patient regardless of delivery system "environment". It is we, and not they, who live with the consequences of substandard care when autonomous decision making is compromised and a negative outcome ensues.

Freedom of choice must also be retained by the patient. It must be possible for patients to choose to return to a doctor who has always provided them with good care and with whom they have a long standing relationship. That is after all what good medicine is all about. Regulations and paperwork that obstruct rather than assist or promote the delivery of good care must be eliminated . Cost of premiums must be reflected in the provision of care to the patients rather than increased profits for insurers. And we *must* find a way to adequately care for *all* patients whatever their circumstance.

It is time for physicians to take back health care. To come together and find our voice to address the challenge of reform within the highest traditions of ethical medical practice. To defend, on behalf of our patients and ourselves, the integrity of our profession and its practice. We can not be demoralized into paralysis or terrorized into deal-making. We must heal divisions between physicians, and between physicians and patients. We must voice our outrage, and assume stewardship of our profession. We are not powerless unless we allow ourselves to be so. We must join together in physician, not hospital- or insurer-run groups. We must provide the leadership rather than be lead.

Most of us would never think of ourselves as heroes, but we have been heroes to our patients and they have been robbed of this image of us that warmed a gentler time. But what is our daily reality? Have our patients lost their heroes or just that vision of us? What really matters to us and keeps us at it when we are disheartened and exhausted and in ERs in the middle of the night?

We are doctors. We came to practice believing that we could make a difference. We have cared for and comforted our patients at moments in their lives of greatest vulnerability-as they deal with the illness of their small child, the death of their spouse, as they confront their own mortality. We have responded to beepers that take us out of our churches and out of our beds, away from our children's soccer fields and our families' tables. Our spouses mark birthdays and holidays without us as we help send patients home to celebrate with theirs. We are physicians. We need to believe in ourselves and our profession and to feel pride and satisfaction in its practice again.

While we address our obligation to the economic future of the health care system through measures that help us to provide excellent cost-effective care such as outcome studies and physician-driven data-based guidelines, we must find answers together that address the challenges that face us all.

> *"If I keep this oath faithfully, may I enjoy my life and practice my art, respected by all men and in all times, but if I swerve from it or violate it, may the reverse be my lot ."*
>
> – The Hippocratic Oath

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Things to do today!

1. Improve our cash flow'
2 Reduce our billing expenses!
3 Increase efficiency in office
4 Eliminate payroll expense for vacations. sick leave. training seminars. etc.
5 Reduce first-time rejection rate on claims through electronic filing insurance
6. Reduce per claim costs for filing insurance
7 Challenge all rejected claims.
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Physicians-in-Training in Rhode Island in 1996

Nikki Deary, BA

The Board of Medical Licensure and Discipline was created in 1986 (Title 5, Chapter 37 of the General Laws of the State of Rhode Island) and is responsible for the regulation of all allopathic (MD) and osteopathic (DO) physicians in the state. The Board's purpose is to protect the public through the licensing of appropriate individuals who meet certain criteria, through the investigation and adjudication of allegations of "unprofessional conduct" and through the dissemination of disciplinary information to health care facilities and to the public at large.

The licensing activities of the Board consist of the issuance of initial full licenses, the yearly re-registration of full licenses and the issuance of limited licenses. The statutory requirements of the Board's enabling legislation, and its regulations and policies, require the receipt of specific documentation regarding training, continuing medical education, character fitness and previous disciplinary actions in order to determine qualifications for these various types of licensure.

LIMITED LICENSURE

Sections 5-37-16 and 16.1 of the Rhode Island General Laws grant authority to the Board of Medical Licensure and Discipline to issue limited licenses to physicians to practice medicine within a recognized, licensed health care institution or hospital as an intern, resident, fellow or medical officer. In addition, the Board may issue a limited registration for an academic faculty member. This type of registration may be issued to a physician of noteworthy and recognized professional attainment, who is an outstanding physician and who has been offered by the dean of a medical school in this state a full-time academic appointment.

Limited training licenses are issued to physicians who are enrolled in the Brown University School of Medicine Residency Training Program as interns, residents and fellows. State law requires that the training hospitals secure the training licenses through the Board and must assure, by appropriate documentation, that the applicants are graduates of medical schools approved by the World Health Organization. State law requires also that graduates of medical schools outside of the United States and Canada must present evidence of certification by the Educational Commission for Foreign Medical Graduates.

In addition, a limited medical officer license may be issued to physicians-in-training who desire to work outside of the scope of the official training program at a hospital or other licensed health care facility. Each hospital/facility must submit an application for issuance of a medical officer license in which the duties of the medical officer are delineated and the identity of the supervising, fully-licensed physician is noted. A trainee may be issued a maximum of 3 medical officer licenses overall in the State of Rhode

TABLE 1

LICENSES ISSUED TO PHYSICIANS-IN-TRAINING IN RHODE ISLAND IN 1996:

HOSPITAL/FACILITY ASSIGNMENTS

	TYPE OF LICENSE				
Facility	Intern	Resident	Fellow	Medical Officer	Total
BLOCK ISLAND MED. CTR.	0	0	0	1	1
BUTLER HOSPITAL*	6	34	0	0	40
LANDMARK MEDICAL CENTER	0	0	0	9	9
MEMORIAL HOSPITAL*	22	50	1	0	73
MIRIAM HOSPITAL*	24	41	5	40	110
RHODE ISLAND HOSPITAL*	82	250	55	74	461
ROGER WILLIAMS HOSPITAL*	15	33	26	22	96
SLATER HOSPITAL	0	0	0	12	12
ST. JOSEPH HOSPITAL	0	0	0	12	12
VETERANS ADMIN. HOSPITAL*	0	1	0	5	6
WOMEN & INFANTS HOSPITAL*	5	19	9	10	43
TOTAL	**154**	**428**	**96**	**185**	**863**

*Brown University Affiliated Training Hospital

TABLE 2

PHYSICIANS-IN-TRAINING
LICENSED IN RHODE ISLAND IN 1996:

AGE AND GENDER

Age Interval (years)	Male	Female
23 - 30	192	161
31 - 40	191	95
41 - 50	28	9
51 - 60	1	1
TOTAL	**412**	**266**

Island and must hold a valid and current intern, resident or fellow training license at the time of issuance of the medical officer license.

The issuance of limited licenses in Rhode Island coincides primarily with the July 1st - June 30th training year in the Brown University Training Hospitals. In 1996, the Board issued 863 limited licenses (intern, resident, fellow and medical officer) for 678 physicians-in-training. Table 1 reflects a breakdown, by facilities of assignment, of the types and quantities of limited licenses issued to trainees during this most recent licensing cycle. The greatest percentage of trainees, 57%, are licensed through, and are assigned at, Rhode Island Hospital. No limited faculty licenses were issued in 1996.

Age and Gender

Table 2 summarizes the distribution of age and gender of the 678 physicians-in-training currently licensed by the Board of Medical Licensure and Discipline. Physicians-in-training who were born from 1966 through 1973 comprise 52% of the current trainee population.

Excepting the 51-60 year old grouping of one male and one female, the percentage of females in each age grouping increases steadily with decreasing age, from 24% of the 41-50 age group, to 33% of the 31-40 age group, to 46% of the 23-30 age group. The percentage of males, *pari passu*, declines from a high of 76% of the physicians-in-training in the age group 41-50, to 67% of the 31-40 year age group, to 54% of 23-30 year olds.

Place of Birth

Table 2 represents both a rank listing and geographic listing of the place of birth of the 678 physicians-in-training. The rank listing indicates the numerical tabulation of the trainees' nation of birth, while the geographic listing reflects a breakdown of states of birth of those trainees born in the United States.

Fifty-eight percent of the currently licensed physicians-in-training were born in the United States. Trainees born in Asia comprise the next greatest percentage grouping at 20%.

Of the 391 physicians-in-training who were born in the United States, 167 (43%) were born in the Middle Atlantic region (New York, Pennsylvania, New Jersey, Maryland, Virginia and Washington, D.C). New England natives comprise 29% of the American-born group, including 32 Rhode Island-born trainees, who comprise less than 5% of the total limited license population.

Medical School Location

The geographic locations of the medical schools of graduation are summarized in Table 4. Approximately 69% have graduated from U.S. or Canadian schools, with slightly less than 34% of that group from New England medical schools. Of the 450 trainees who are graduates of United States medical schools, 372 (83%) were born in this country.

Once again, Asian countries have contributed significantly to the Rhode Island trainee population with 92 physicians-in-training (14%) having graduated from Asian medical schools.

TABLE 3

PHYSICIANS-IN-TRAINING
LICENSED IN RHODE ISLAND IN 1996:

PLACE OF BIRTH

Rank Listing		Geographic Listing (USA)	
391	USA	Massachusetts	56
50	INDIA	Rhode Island	32
22	PHILIPPINES	Connecticut	22
19	PAKISTAN	Maine	2
16	CANADA	Vermont	2
13	CHINA	New Hampshire	1
12	JORDAN	NEW ENGLAND STATES TOTAL	115
7	TAIWAN		
7	SOUTH KOREA	New York	95
7	LEBANON	Pennsylvania	28
6	EGYPT	New Jersey	27
6	RUSSIA	Maryland	10
5	GHANA	Virginia	5
5	MEXICO	Washington D.C.	2
5	ENGLAND	MID ATLANTIC STATES TOTAL	167
4	BANGLADESH		
4	ITALY	Midwestern States	43
4	VIETNAM	Pacific States	23
4	TURKEY	North Central States	21
4	ROMANIA	Southern States	12
4	HONG KONG	Mountain States	9
4	SYRIA	Puerto Rico	1
70	Physicians-in-Training from 47 other Countries	ALL OTHERS	109

YEARLY GROWTH

The number of limited licenses issued by the Rhode Island Board of Medical Licensure and Discipline has increased steadily since 1992. During 1992, 567 licenses were issued for interns, residents, fellows and medical officers. In 1993, the number of such licenses issued increased to 624, followed by 672 in 1994, 767 in 1995, and 863 in 1996. Over the period 1992-1996, there was an annual average increase of 11% in the number of limited licenses issued in the state.

Due to the growing numbers of medical school graduates accepted into the Brown University Training Program, the Board has developed more rigorous systems with which to evaluate and license physicians-in-training. A great deal of credit for the ongoing upgrading and resultant successes of this regulatory program must be attributed to the Brown University Training Program, as well as the licensed health care facilities who play an integral role in this process.

THE NATIONAL SCENE

The level of regulation of physicians-in-training by state medical boards varies considerably. According to the Federation of State Medical Boards of the United States, Inc. *1995-96 Exchange,* 13 of the 63 member state medical boards (including, in some states, separate boards for allopathic and osteopathic physicians) require a full, unrestricted license for their physicians-in-training, 37 boards require some form of limited licensure and 13 medical boards have no process in place for the regulation of this population.[1,2] The Rhode Island Board stands in the forefront of the stated goal of the Federation of State Medical Boards to encourage licensure of physicians-in-training in all states.

TABLE 4

PHYSICIANS-IN-TRAINING
IN RHODE ISLAND IN 1996:

LOCATION OF MEDICAL SCHOOL OF GRADUATION

Rank Listing		Geographic Listing	
450	USA	Mid Atlantic States	171
32	INDIA	New England States	159
25	PHILIPPINES	Midwestern States	61
18	CANADA	North Central States	28
17	PAKISTAN	Canada	18
12	CHINA	Southern States	17
11	JORDAN	Pacific States	10
7	LEBANON	Mountain States	4
7	RUSSIA	**USA & CANADA TOTAL**	**468**
6	MEXICO		
6	GRENADA		
5	DOMINICAN REPUBLIC	Asia	92
5	ITALY	Europe	38
5	EGYPT	Near East	34
5	GHANA	Latin America*	26
4	TURKEY	Africa	9
4	GERMANY	New Ind Sts Frmr Soviet	9
4	BULGARIA	Australia	1
4	ROMANIA	**OTHERS TOTAL**	**209**
4	BANGLADESH		
46	PHYSICIANS-IN-TRAINING FROM 32 OTHER COUNTRIES		

* Includes Caribbean Island medical schools

Nikki Deary, BA, is the Deputy Chief Administrative Officer of the Board of Medical Licensure and Discipline, Rhode Island Department of Health.

REFERENCES

1. *1995-1996 Exchange,* Section 1, USMLE and M.D. Licensing Requirements. Euless, Texas: Federation of State Medical Boards of the United States, Inc., 1995: Table 59, page 89.
2. *1995-1996 Exchange,* Section 1, USMLE and D.O. Licensing Requirements. Euless, Texas: Federation of State Medical Boards of the United States, Irc., 1995: Table 49, page 73.

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PUBLIC HEALTH BRIEFING

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by John P. Fulton, PhD

Proposed Oral Cancer Screening Recommendations

John Duhaime, DMD, and Joann Lindenmayer, DVM, MPH

Objective

The Rhode Island Department of Health assembled an Expert Panel on Cancer Screening to advise the Department on revising the State's current cancer control plan, published in 1989.

After reviewing the current screening recommendations of national organizations and the most recent pertinent literature, the Panel proposed a recommendation for oral cancer screening.

Methods

- Review current oral cancer screening recommendations of national organizations.
- Review the most recent literature pertinent to oral cancer screening.
- Discuss.
- Propose an oral cancer screening recommendation for the State's cancer control plan.
- Write a simple rationale for the proposed oral cancer recommendation.
- Invite comments on the proposed recommendation and rationale.

Current Recommendations

Organization	Recommendations
U.S. Preventive Services Task Force[2]	• Does not recommend for or against routine screening of asymptomatic persons for oral cancer by primary care clinicians. • Clinicians should remain alert to signs and symptoms of oral cancer and premalignancy in persons who use tobacco or alcohol.
National Cancer Society	• Recommends a cancer checkup that includes an oral examination every 3 years for persons over age 20, and annually for persons over age 40.
Canadian Task Force on the Periodic Health Examination	• Does not recommend for or against screening for oral cancer in the periodic health examination. • Suggests that annual oral examination by a physician or a dentist should be considered for persons over 60 with risk factors for oral cancer (smokers and regular drinkers).
National Cancer Institute	• No specific guidelines. • Supports efforts to promote the early detection of oral cancer during routine dental examinations.
National Institute of Dental Research	• No specific guidelines. • Supports efforts to promote the early detection of oral cancer during routine dental examinations.

Proposed Recommendations

- There is sufficient evidence to recommend that primary care providers [primary care providers refers in all cases to medical and dental primary care providers] perform a complete oral cancer screening examination on all patients who use tobacco, alcohol, or both, regardless of age, whenever the oral cavity is examined.
- Primary care providers should screen all patients over the age of 65 whenever the oral cavity is examined.
- Primary care providers should remain alert to the signs of early oral cancer, particularly leukoplakia and erythroplakia, and should refer patients with these lesions to a surgical specialist for further evaluation and treatment.

Rationale

When the Rhode Island Cancer Control Plan for 1990-1992 was published, age 35 and above was used to define a group of people at elevated risk for development of oral cancer and for which oral cancer screening was recommended. Recognition of the enormous contribution of tobacco use and alcohol consumption to the development of oral cancer has led the Cancer Control Advisory Group to recommend further refinement of the target group for screening to include users of tobacco and/or alcohol. The rationale for departing from the U.S. Preventive Services Task Force recommendations, and for changes to the previous R.I. Cancer Control Plan, took the following into account:

- Oral health problems, including oral cancer, represent a common chronic health problem in the population. The majority of oral cancers are diagnosed in advanced stages of disease.
- Detection and treatment of small, localized lesions is associated with significantly higher 5-year survival rates, and significantly less disfigurement, than is the case with more advanced lesions.
- More than three fourths of all oral cancers occur in locations that are accessible to visual examination or digital palpation.
- 90% of oral cancers occur in persons 40 years of age and over. 50% of all oral cancers, and the majority of deaths from oral cancer occur in persons 65 years of age and over.
- Tobacco in all forms and excessive consumption of alcohol are independent and synergistic risk factors for oral cancer, regardless of a person's age. Nearly 70% of deaths from oral cancer are associated with smoking and other forms of tobacco use, and 90% of all oral cancers are attributed to the combined effects of tobacco and alcohol.
- Current screening practices for oral cancer reach less than 15% of the population. Patients at any age, but particularly the elderly, are more likely to seek medical rather than dental care. Physicians have many opportunities to identify suspect oral lesions at an early stage and to refer patients to an appropriate specialist.

Comments?

We invite your comments on the proposed recommendation and rationale. Please send them in writing to Dr. Joann Lindenmayer by fax (401-861-5751) or mail (Rhode Island Department of Health, 3 Capitol Hill, Providence, RI 02908-5097).

References

1. Rhode Island Department of Health. *Cancer Control Rhode Island. Plan for 1990-1992.* Providence, RI: Rhode Island Department of Health, 1989.
2. U.S. Preventive Services Task Force. *Guide to Clinical Preventive Services, 2nd ed.,* Baltimore: Williams and Wilkins, 1996.

John Duhaime, DMD, is a dentist in private practice.

Joann Lindenmayer, DVM, MPH, is Chronic Disease Epidemiologist, Rhode Island Department of Health, and Clinical Assistant Professor, Department of Community Health, Brown University Medical School.

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Vital Statistics

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health
Edited by Roberta A. Chevoya

Rhode Island Monthly Vital Statistics Report
Provisional Occurrence Data from the Division of Vital Records

Vital Events

	Reporting Period		
	June 1996	**12 Months Ending with June 1996**	
	Number	**Number**	**Rates**
Live Births	1,065	14,001	14.1*
Deaths	704	9,636	9.7*
Infant Deaths	(9)	(98)	7.0#
Neonatal deaths	(9)	(77)	5.5#
Marriages	1,063	7,994	8.0*
Divorces	240	3,419	3.4*
Induced Terminations	559	5,550	396.4#
Spontaneous Fetal Deaths	54	1,096	78.3#
Under 20 weeks gestation	(52)	(1,048)	74.9#
20+ weeks gestation	(2)	(48)	3.4#

* Rates per 1,000 estimated population
# Rates per 1,000 live births

Underlying Cause of Death

	Reporting Period			
	December 1995	**12 Months Ending with December 1995**		
	Number (a)	**Number (a)**	**Rates (b)**	**YPLL (c)**
Diseases of the Heart	310	3,336	334.8	4,263.5
Malignant Neoplasms	243	2,535	254.4	6,528.5
Cerebrovascular Diseases	68	656	65.8	587.5
Injuries (Accident/Suicide/Homicide)	35	333	33.4	6,371.0
COPD	41	419	42.1	395.0

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.
(b) Rates per 100,000 current estimated population of 996,325
(c) Years of Potential Life Lost (YPLL)

Note: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

THE RHODE ISLAND MEDICAL JOURNAL

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NINETY YEARS AGO

[NOVEMBER, 1906]

The proceedings of the regular meeting of the Providence Medical Association for October 1, 1906, are published. They deal principally with an extended inquiry into the clinical presentations, epidemiological features, prognostic elements, surgical statistics and bacteriologic studies of acute appendicitis. Dr. Charles V. Chapin presents his experience with this disorder which includes 292 cases observed over an interval of 16 years. Chapin is impressed with the fact that the number of deaths per year ascribable to appendicitis has risen dramatically between 1886 and 1906 [from 0 per 100,000 to 17/100,000 population.] Part of the reason, he speculates, may be that appendicitis deaths, in the past, likely were called fatal peritonitis [he reminds his audience that the famous paper by R. Fitz describing the clinical and surgical features of the disease only appeared in 1886.] It is possible, too, that cases may have been called by still other names [eg, colic]. But even if one considers all cases of peritonitis and all cases of intestinal disease of unknown etiology as appendicitis, there still seems to be a rise in the incidence of this disorder.

There was much discussion on the means by which appendicitis may be rapidly diagnosed. Right lower quadrant pain and rigidity, vomiting, fever and an elevated white blood cell count were all mentioned.

Dr. Marshall Fulton then summarizes his laboratory experience with appendicitis, noting that the mortality rate with acute perforation is higher, but not much higher, than cases without perforation. He expresses the belief that the nature of the suppurating organism, as well as the presence or absence of perforation, plays a significant prognostic role. He provides the audience with some data concerning the role of streptococci and the coliform organisms in this disease.

The health statistics for the city of Providence are provided by its Superintendent of Health, Dr. Charles V. Chapin. His report notes that the number of deaths had risen in both August and September when compared to the same months in 1905. He could offer no reason for this elevation. The weather during the summer of 1906 "was such as usually causes an increase in diarrheal diseases," and indeed the number of deaths from this cause had increased to 203. The number of cases of scarlet fever [39], diphtheria [25] and typhoid fever [104] had risen appreciably. Many of the cases of typhoid fever had been traced to two milk suppliers. During this summer interval, 14 rabid dogs and 3 rabid cats had been identified by laboratory means. There were 15 persons bitten by rabid animals and all but one submitted to the Pasteur therapy. There was one death from rabies in the town of Johnston.

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Medicine & Health
RHODE ISLAND

Published monthly by the Rhode Island Medical Society under the joint editorial sponsorship of Brown University School of Medicine and the Rhode Island Department of Health.

FIFTY YEARS AGO

[DECEMBER, 1946]

The lead contribution is a speech by Shields Warren, MD, on the medical aspects of the atomic bombings, presented before the Providence Medical Association on November 4, 1946. [Dr. Warren was Executive Officer, Naval Medical Research Section of Operation Crossroads.] Dr. Warren's presentation considered two aspects of atomic energy: first, as a tool for biomedical research; and second, as a hazard for humanity as a whole. After reviewing some of the more recent applications of radioactive tags in clinical research, he then dwelt at length upon the devastating effects of an atomic bomb explosion upon the residents of Hiroshima and Nagasaki. He concludes with this personal reflection: "I thought it too bad we didn't just drop it [ie, the atomic bomb] on the herds up in Hokkaido as a demonstration. However, when I talked to some of the leading Japanese they told me that the dropping of the bombs actually saved many Japanese lives as well as many American lives and they were glad it had been dropped. To surrender to ordinary warfare would be to lose face. "

Theodore G. Klumpp, MD, President of Winthrop Chemical Company, talks of the future of medical research, concentrating his remarks on such problems as dental caries, cancer and human longevity. He concludes his paper with a plea for more competition in the arena of medical research. "Our great industrial achievements were built on competition and we must take a leaf from this notebook and apply it to medical research. Government research is conducted under the sway of of the classical philosophy that there can be no competition with government. If necessity is the mother of invention, its father is competition."

TWENTY FIVE YEARS AGO

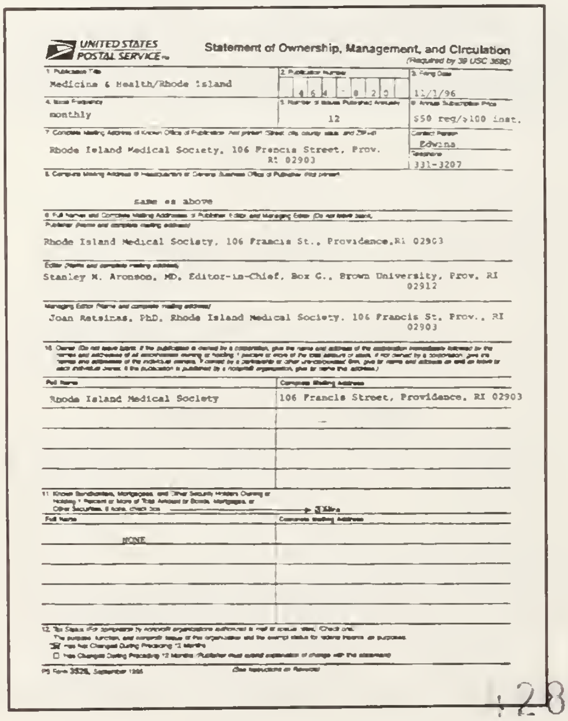
[DECEMBER, 1971]

Mary Lekas, MD, presents the case of an 11 year old boy who had developed severe complications from a recently administered smallpox vaccination [it had been delayed from early childhood because of his concurrent eczema.] He developed satellite vaccinial lesions of the left nostril with an associated purulent sinusitis. In addition to antibiotics the patient was given hyperimmune vaccine gamma globulin and within 24 hours the patient's lesions began to clear and his temperature returned to normal.

A retrospective analysis of maternal mortality in Rhode Island during the years 1965 to 1969 is presented by Stanley D. Davies, MD, J. Kenneth Beezer, MD, and John R. Evrard, MD. During this hemi-decade, there were 27 maternal deaths in 80,061 live birth deliveries. Of these 27, 11 were obstetrical deaths [2 from hemorrhage, 7 from infection, and 2 from pulmonary emboli.] The overall maternal mortality rate is essentially unchanged when compared with the preceding half decade.

Lawrence A. Senseman, MD, describes alcohol as a major health hazard and makes a plea that programs encouraging voluntary prohibition of alcohol be instituted.

An editorial decries the efforts of some Brown University faculty who would stifle the beginnings of a medical education program on campus.



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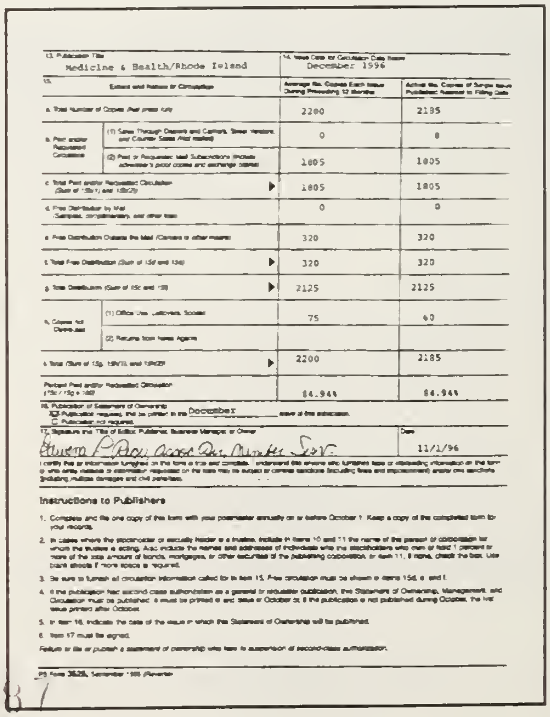

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